

Web Material

To accompany:

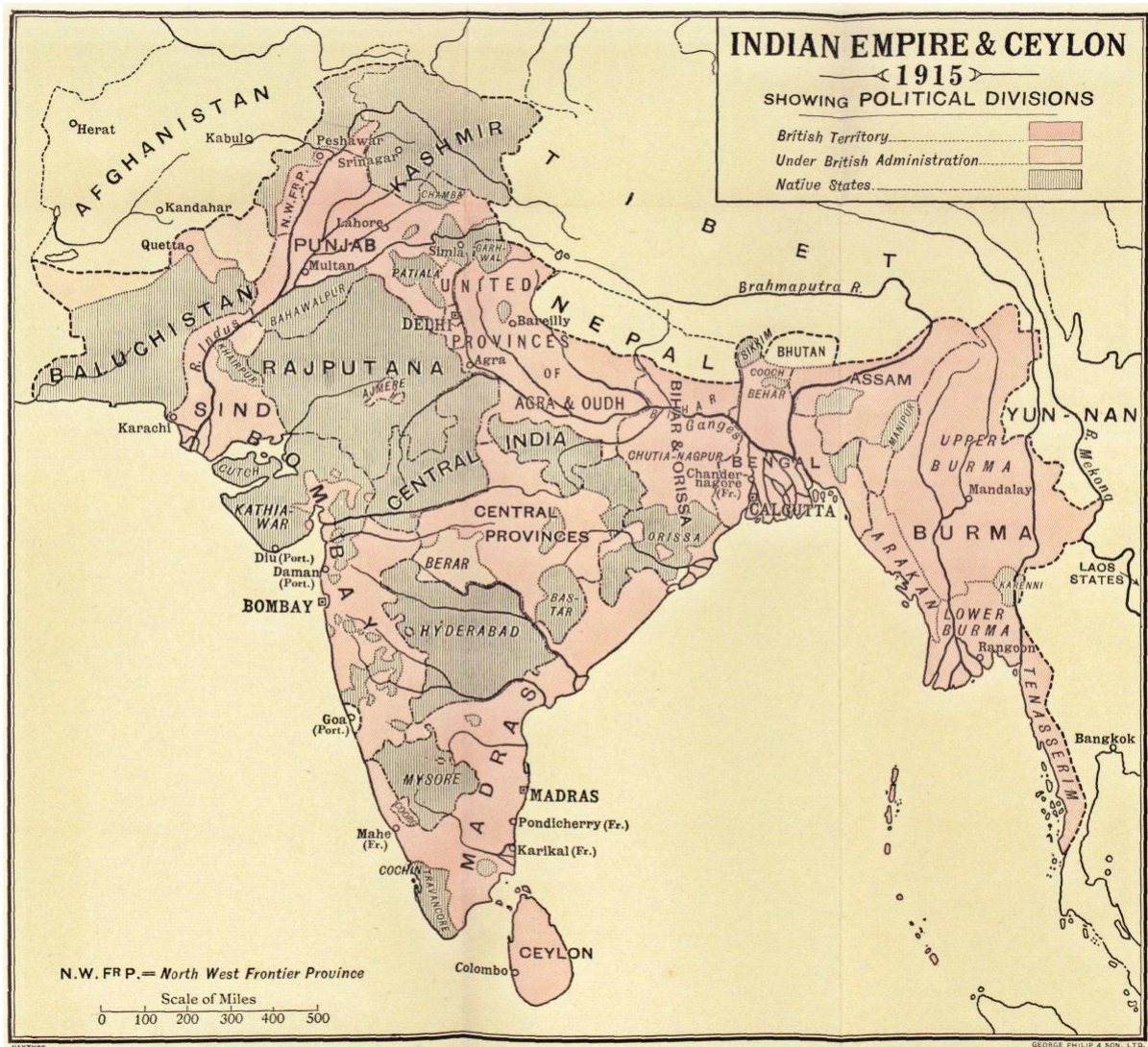
Title: Reassessing the global mortality burden of the 1918 influenza pandemic.

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Web figure 1.



Map of British Indian Empire and Ceylon in 1915 at the end of Vincent Smith's *India in the British Period* (part III, *Oxford History of India*), Oxford: Clarendon Press, 1920.

en.wikipedia

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Web Appendix 1.

The yearly mortality rates, our dependent variable, are nested within countries, hence we used a multilevel model, in which level-2(j) is the country level and level-1(i) is the years within a country.

We included the following predictor variables in every separate age analysis:

- Intercept (coded 1 for every observation), used to model the between and within country variance (random part, level 2 and 1 intercept variance), not used in the fixed part.
- War indicator (coded 1 for observations in 1918 if country was at war in 1918, else 0). Fixed part only. (countries at war in 1918, Finland, France, Italy, UK England-wales, UK Scotland).
- Trend, continuous variable (coded year-1918.5), fixed part and random at level 2 (to allow for countries to have different time trends).
- 1918 indicator (coded 1 for observations if year equals 1918, else 0). Fixed part only.
- 1919 indicator (coded 1 for observations if year equals 1919, else 0). Fixed part only.
- Measurement scenario indicator(s). Three different versions, years look only at 1916,1917,1920,1921 depending on the chosen scenario, and is 0 in the years 1918 1919:

LOW-model

$$\text{Mortality rate}_{ij} = \beta_{10} \text{Year1918}_{ij} + \beta_{20} \text{Year1919}_{ij} + \beta_{30} \text{YearLow}_{ij} + \beta_{40} \text{YearRest}_{ij} + \beta_{01} \text{War1918}_j + \beta_{50} \text{Trend}_{ij} + \mu_{0j} + \mu_{1j} \text{Trend}_{ij} + \varepsilon_{ij}$$

YearLow indicator (coded 1 for year closest to but smaller than the pandemic years). Fixed part only.

Rest year indicator (coded 1 for years 1916 1917 1920 1921 if low indicator equals 0 else 0). Fixed part only.

HIGH-model

$$\text{Mortality rate}_{ij} = \beta_{10} \text{Year1918}_{ij} + \beta_{20} \text{Year1919}_{ij} + \beta_{30} \text{YearHigh}_{ij} + \beta_{40} \text{YearRest}_{ij} + \beta_{01} \text{War1918}_j + \beta_{50} \text{Trend}_{ij} + \mu_{0j} + \mu_{1j} \text{Trend}_{ij} + \varepsilon_{ij}$$

YearHigh indicator (coded 1 for year furthest from but smaller than the pandemic years). Fixed part only. Rest year indicator (coded 1 for years 1916 1917 1920 1921 if high indicator equals 0 else 0). Fixed part only.

MEDIUM-model

$$\text{Mortality rate}_{ij} = \beta_{10} \text{Year1918}_{ij} + \beta_{20} \text{Year1919}_{ij} + \beta_{30} \text{YearMedium}_{ij} + \beta_{01} \text{War1918}_j + \beta_{50} \text{Trend}_{ij} + \mu_{0j} + \mu_{1j} \text{Trend}_{ij} + \varepsilon_{ij}$$

YearMedium indicator (coded (1-0.25,0-0.25) for every observation in the years 1916 1917 1920 1921). Fixed part only.

Estimation World excess rate:

$$\text{Population(world) excess rate 1918} = \beta_{10} - \beta_{30}$$

$$\text{Population(world) excess rate 1919} = \beta_{20} - \beta_{30}$$

Since we don't have the world population data for the different age groups, we first have to estimate total excess deaths, which we calculated as follows:

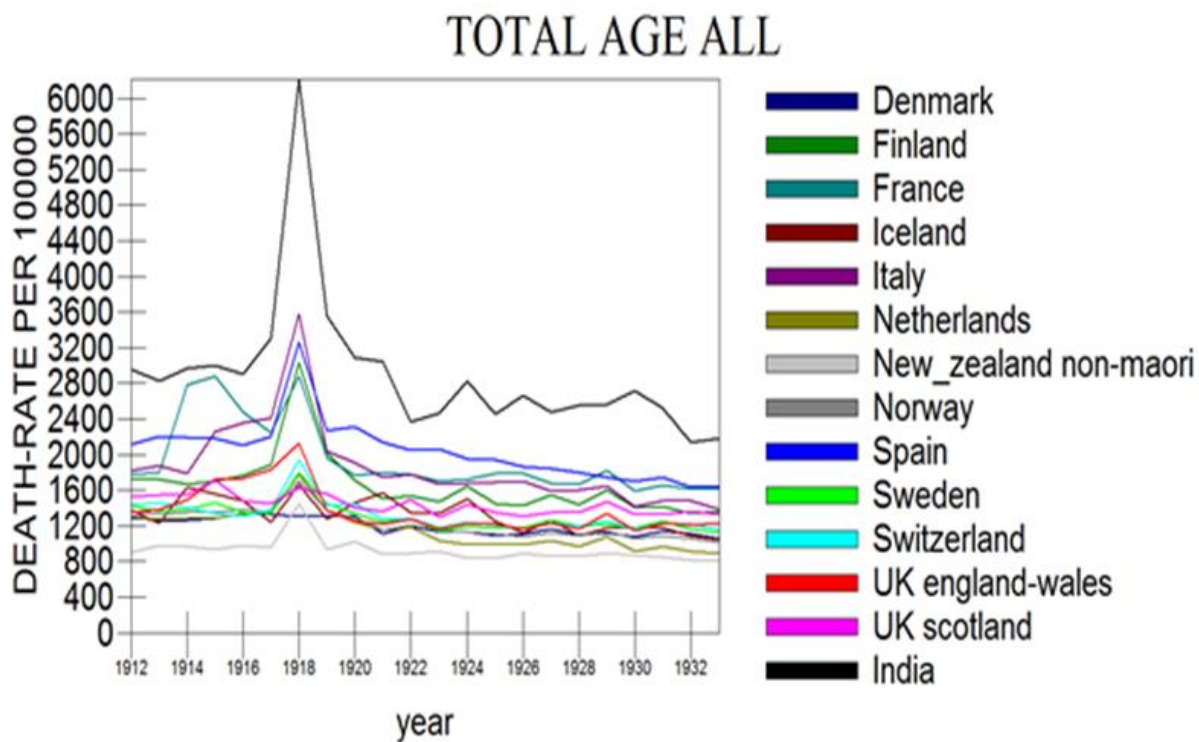
(1918 or 1919 pandemic mortality rate)-(low or high or medium indicator mortality rate)*population, per age group.

Next we summed over all the age groups to get the total excess deaths in the sample. We then divided this by the total sample population to get the average excess mortality rate, which is used as an estimate of the world excess mortality rate in 1918 or 1919. Note that this procedures assumes that in the fixed part the intercept is left out, so the 1918, 1919 and measurement scenario indicators give the average mortality rates, and the difference is the average excess mortality rate due to the pandemic.

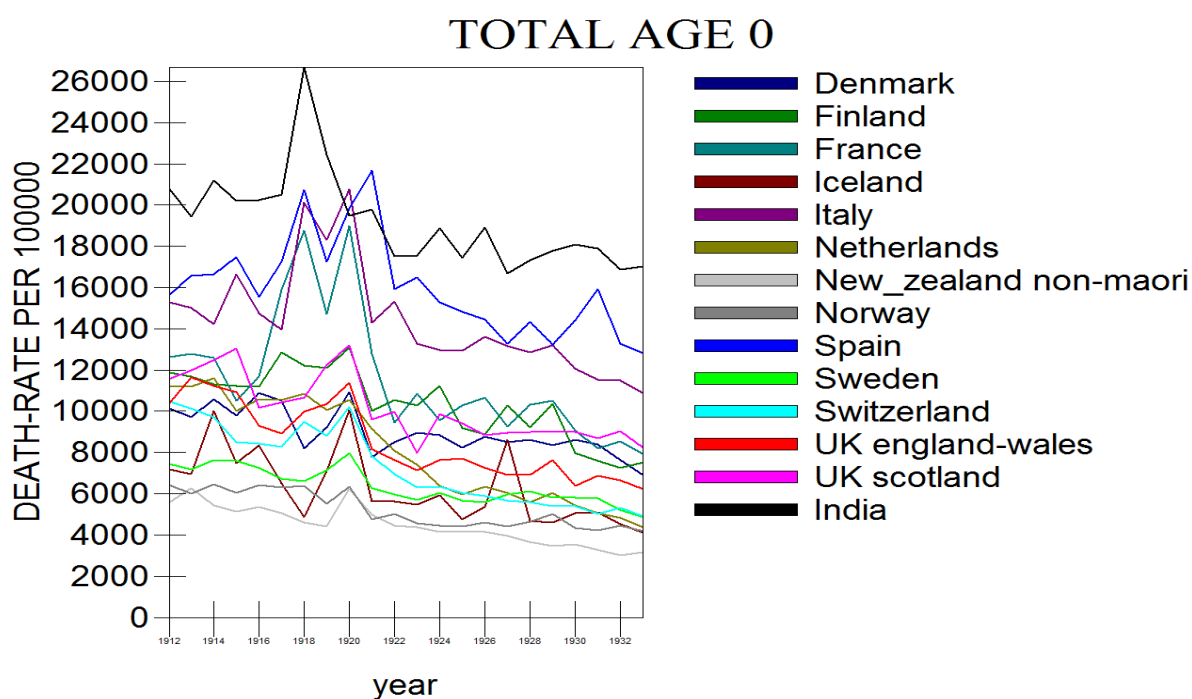
Web Figure 2A-2K.

Observed mortality rates per age group in the sample.

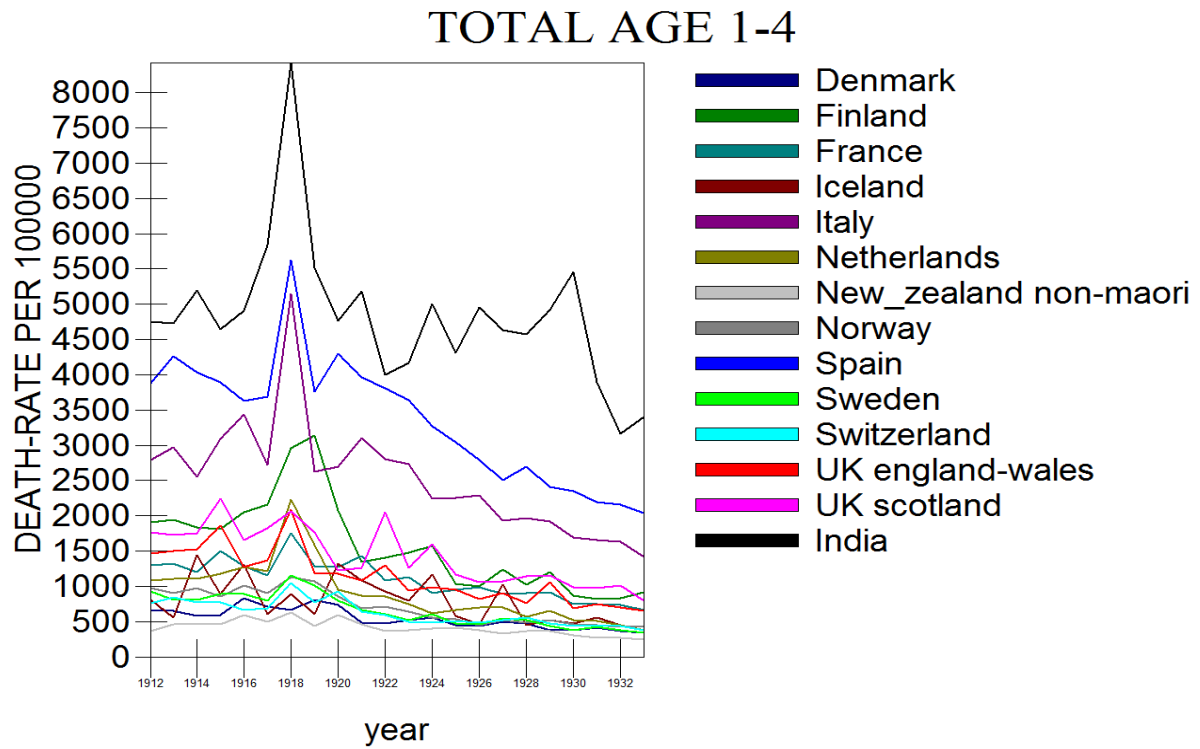
Web Figure 2A



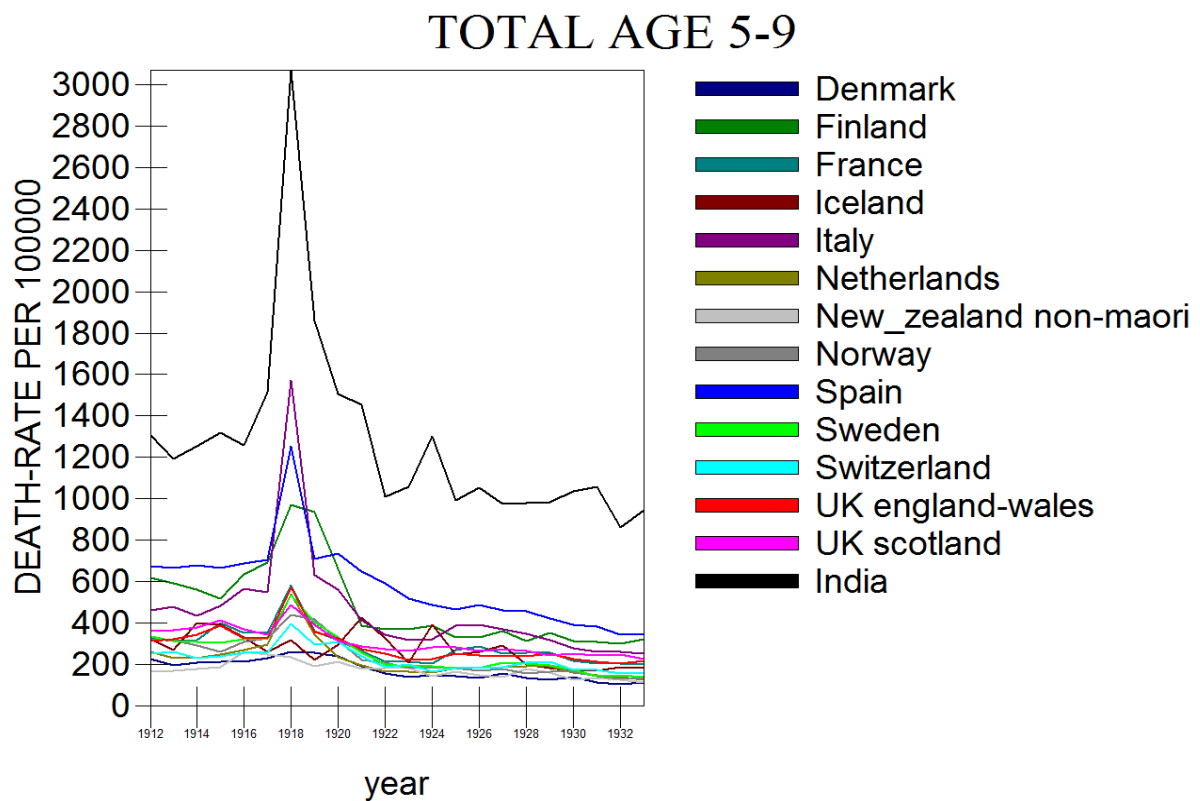
Web Figure 2B



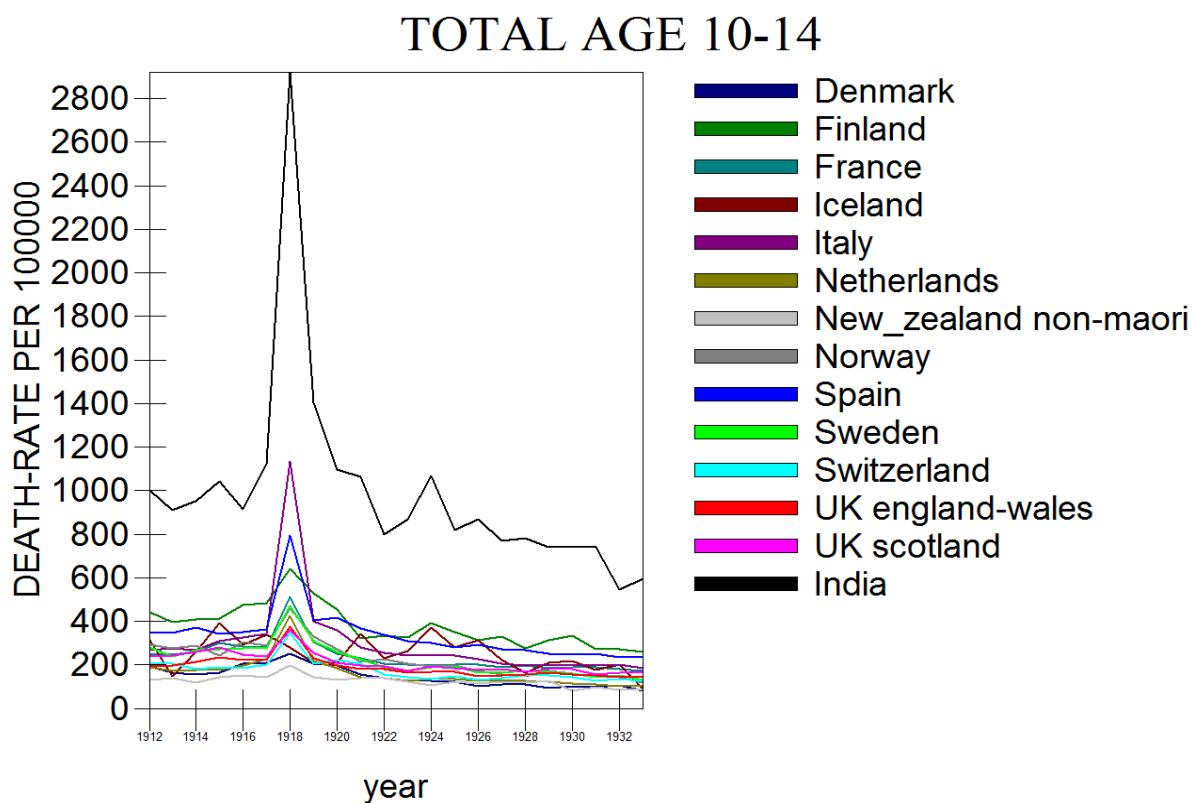
Web Figure 2C



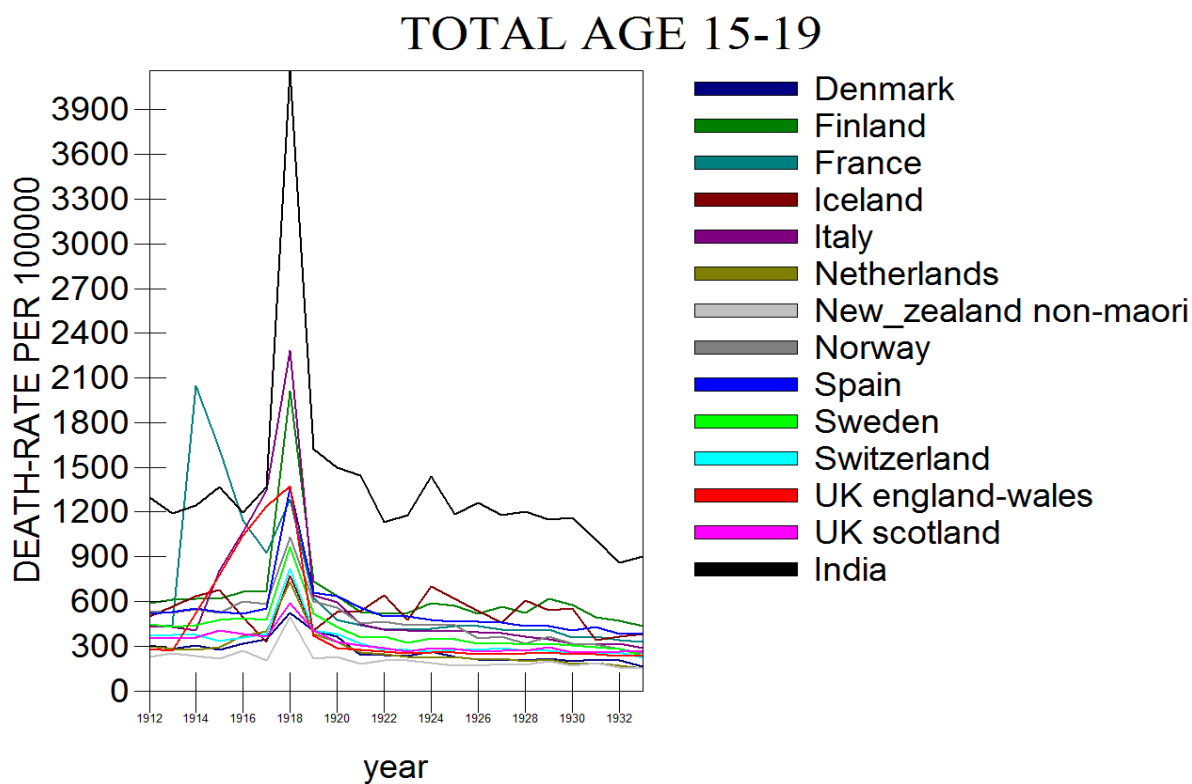
Web Figure 2D



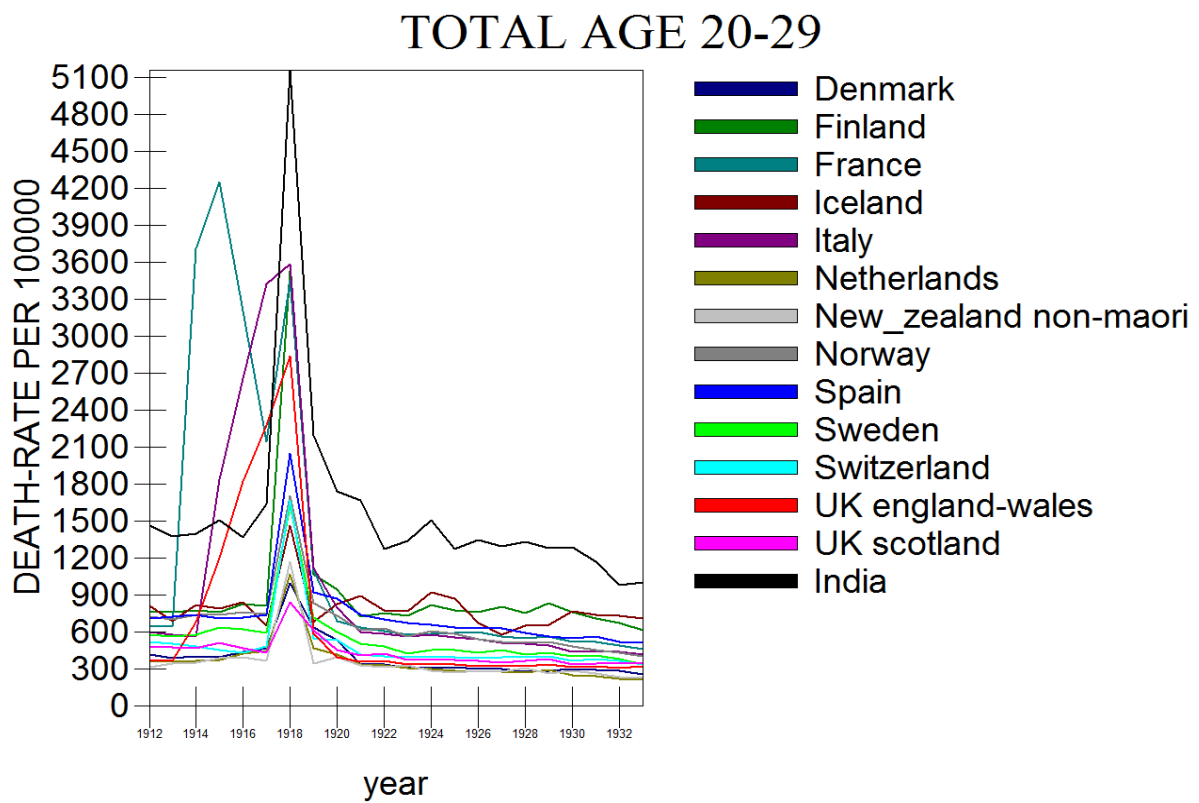
Web Figure 2E



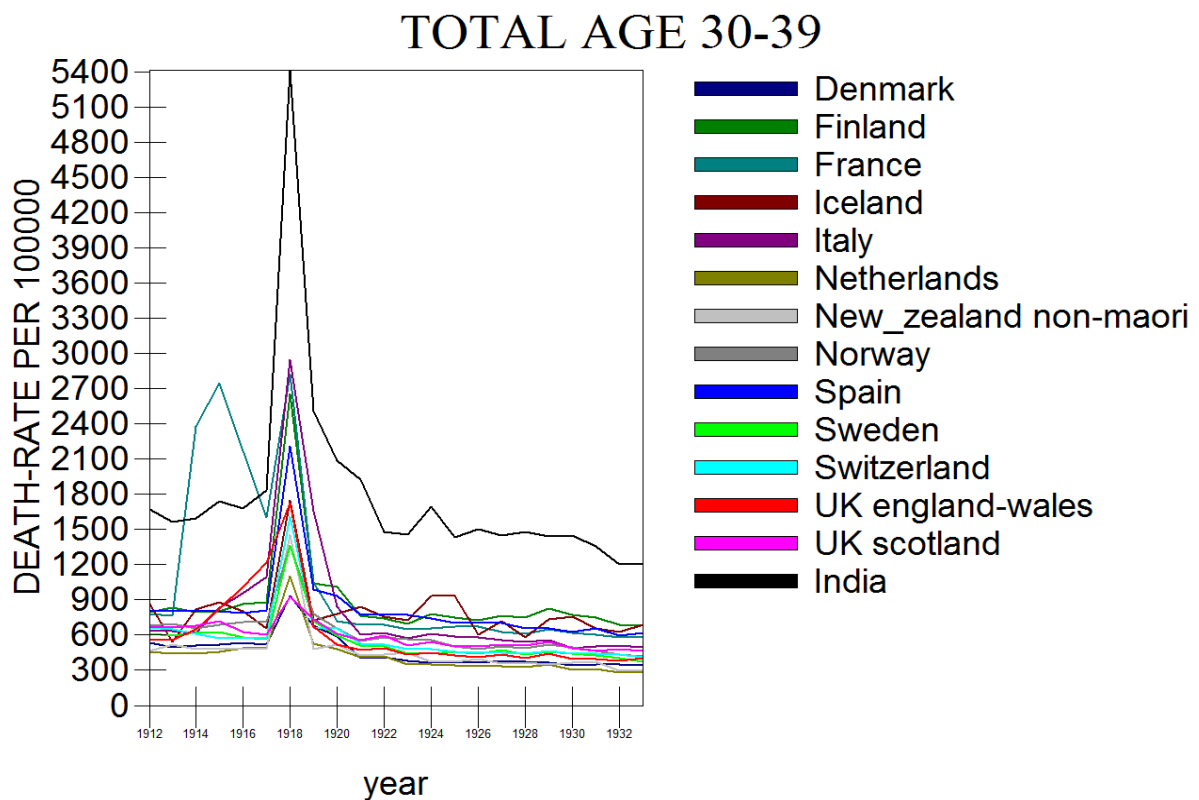
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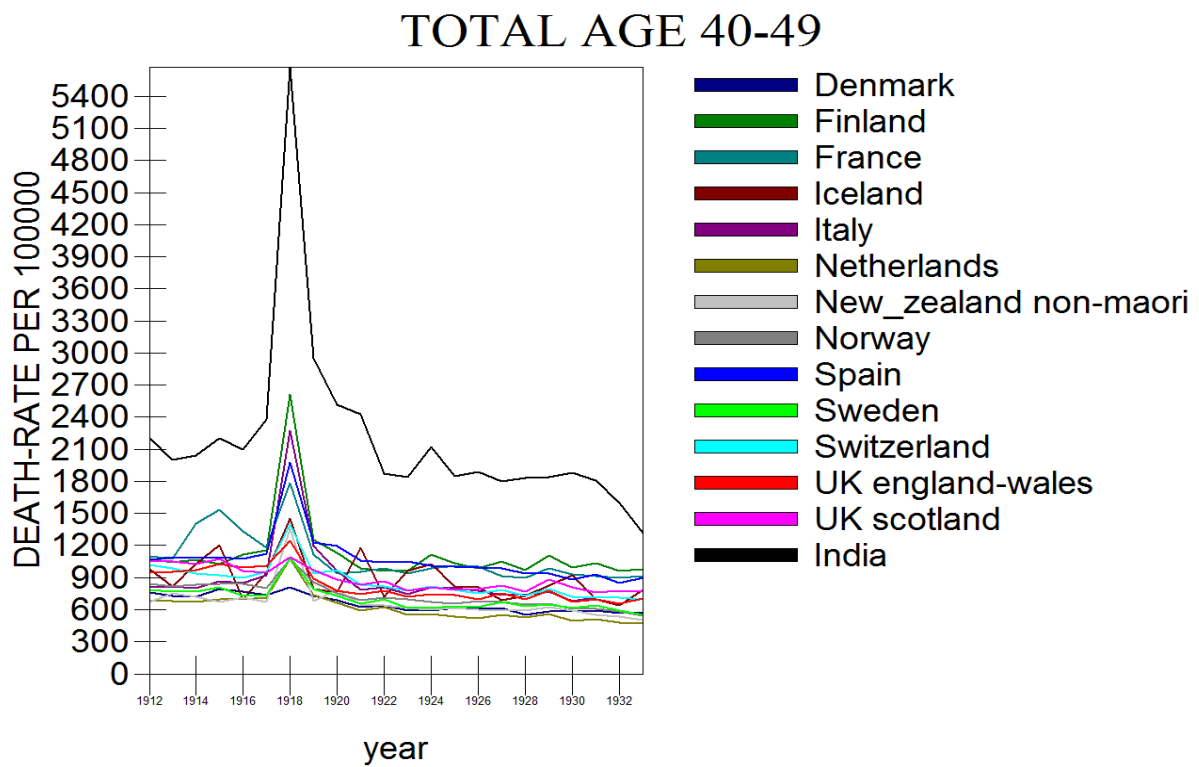
Web Figure 2G



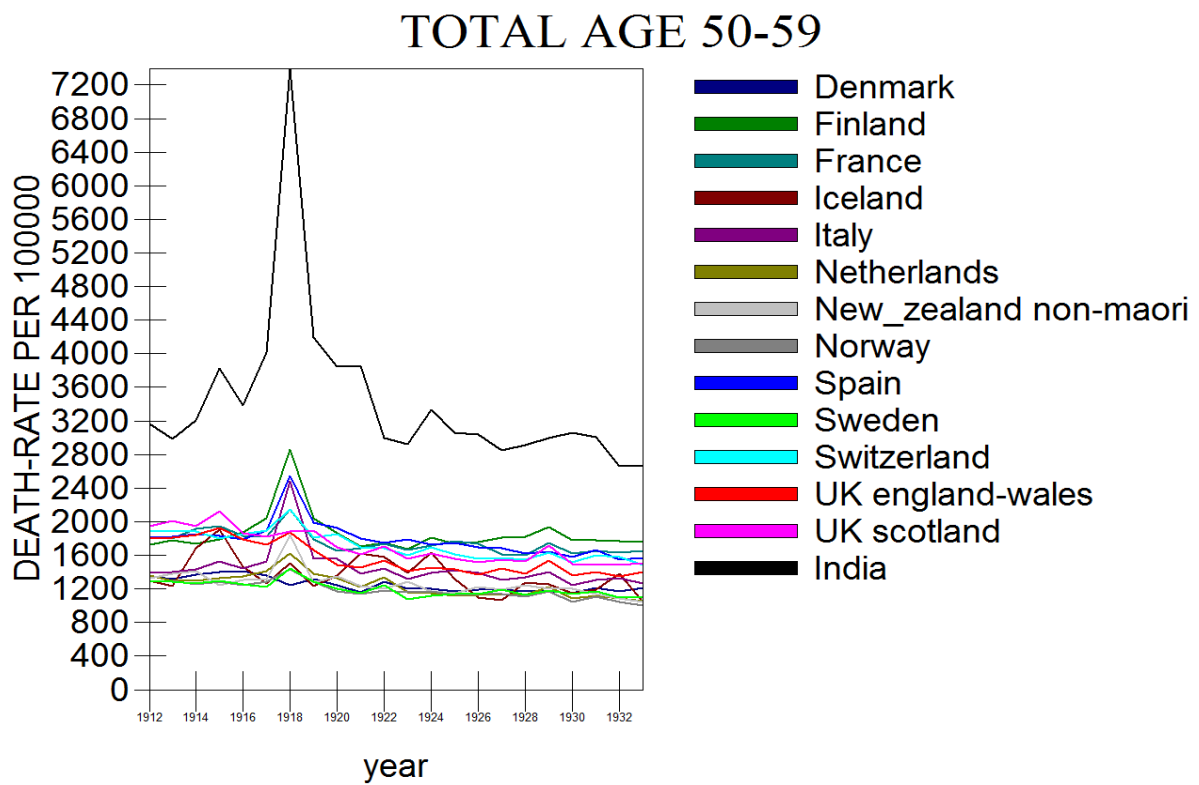
Web Figure 2H



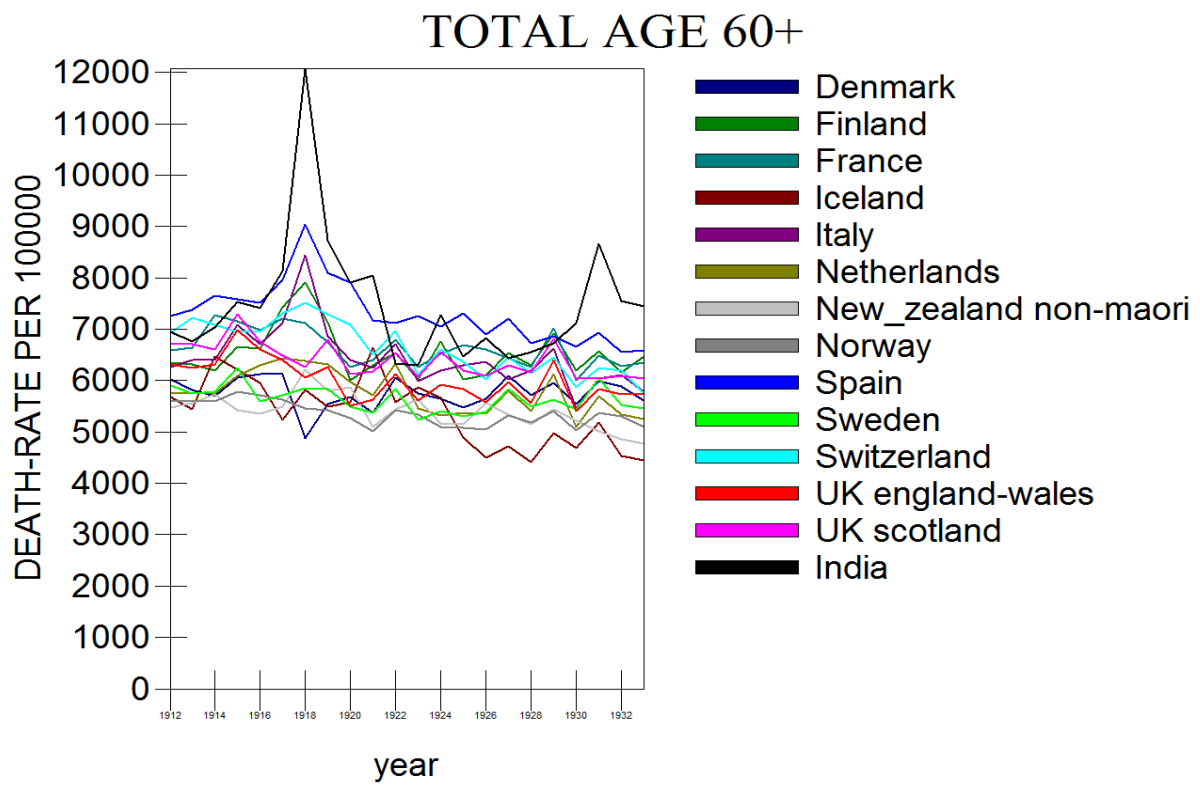
Web Figure 2I



Web Figure 2J



Web Figure 2K



Web table 1A-1B.

Additional sensitivity analysis material for table 1. Analysis based on the HMD data only (without India), with 10 age groups and 20 age groups instead of 10 (0,1-4,5-9,...,85-89,90 and older). In the table for the 20 age groups we also added the results using the direct calculations method.

Web Table 1A

10 AGE CATEGORIES WITHOUT INDIA		LOW		MEDIUM		HIGH	
ESTIMATION STRATEGY	YEAR	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT
MODEL BASED CALCULATION	1918	723.4	13.82M	653.2	12.48M	867.3	16.57M
	1919	122.8	2.37M	65.8	1.27M	266	5.13M
MODEL CORRECTED FOR TIME TREND	1918	679.8	12.98M	630.7	12.05M	785.2	15.0M
	1919	124.7	2.4M	78.1	1.51M	211.4	4.07M
MODEL CORRECTED FOR WAR 1918 AND TIME TREND	1918	510.1	9.74M	463.2	8.85M	617.9	11.8M
	1919	124.7	2.4M	78.1	1.51M	211.4	4.07M

Web Table 1B

20 AGE CATEGORIES WITHOUT INDIA		LOW		MEDIUM		HIGH	
ESTIMATION STRATEGY	YEAR	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT
DIRECT CALCULATION	1918	718.7	13.73M	681.9	13.03M	885.8	16.92M
	1919	119.8	2.31M	113.1	2.18M	269.6	5.2M
MODEL BASED CALCULATION	1918	728.8	13.92M	667.3	12.75M	882.5	16.86M
	1919	123.1	2.37M	74.3	1.43M	276.1	5.32M
MODEL CORRECTED FOR TIME TREND	1918	683.5	13.05M	643.5	12.29M	792	15.13M
	1919	126.7	2.44M	91.6	1.76M	221.6	4.27M
MODEL CORRECTED FOR WAR 1918 AND TIME TREND	1918	507.7	9.70M	472.9	9.03M	616.6	11.78M
	1919	126.7	2.44M	91.6	1.76M	221.6	4.27M

Web Table 2 .

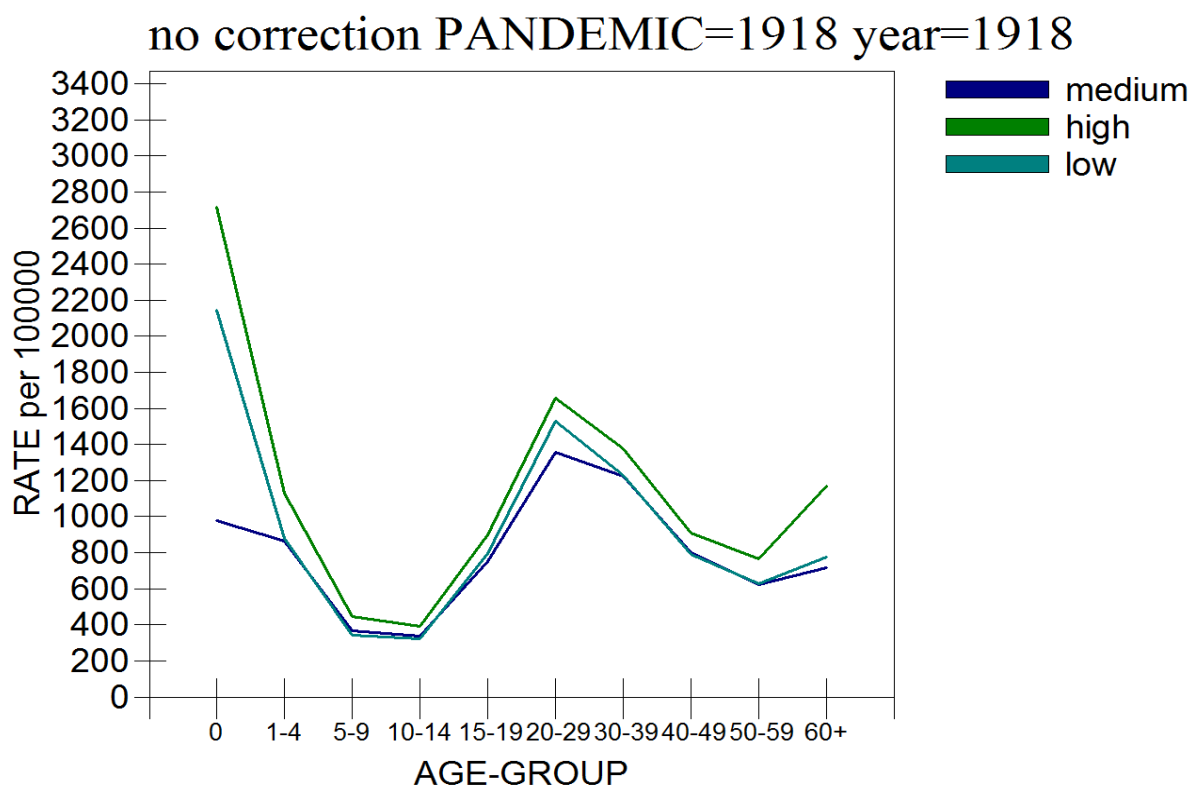
Additional table with monthly excess based on sample data for India only.

MONTH	YEAR	AVERAGE		MONTH	YEAR	AVERAGE	
		EXCESS RATE PER 100000	EXCESS DEATH COUNT			EXCESS RATE PER 100000	EXCESS DEATH COUNT
JAN	1918	69	164564	JUL	1918	30	71549
	1919	82	195555		1919	50	119241
FEB	1918	62	147869	AUG	1918	60	143099
	1919	56	133550		1919	29	69160
MAR	1918	114	271888	SEP	1918	735	1752962
	1919	51	121626		1919	19	45312
APR	1918	99	236113	OCT	1918	1424	3396215
	1919	29	69160		1919	37	88238
MAY	1918	101	240883	NOV	1918	680	1621788
	1919	73	174092		1919	91	217019
JUN	1918	81	193184	DEC	1918	79	188414
	1919	62	147859		1919	196	467425

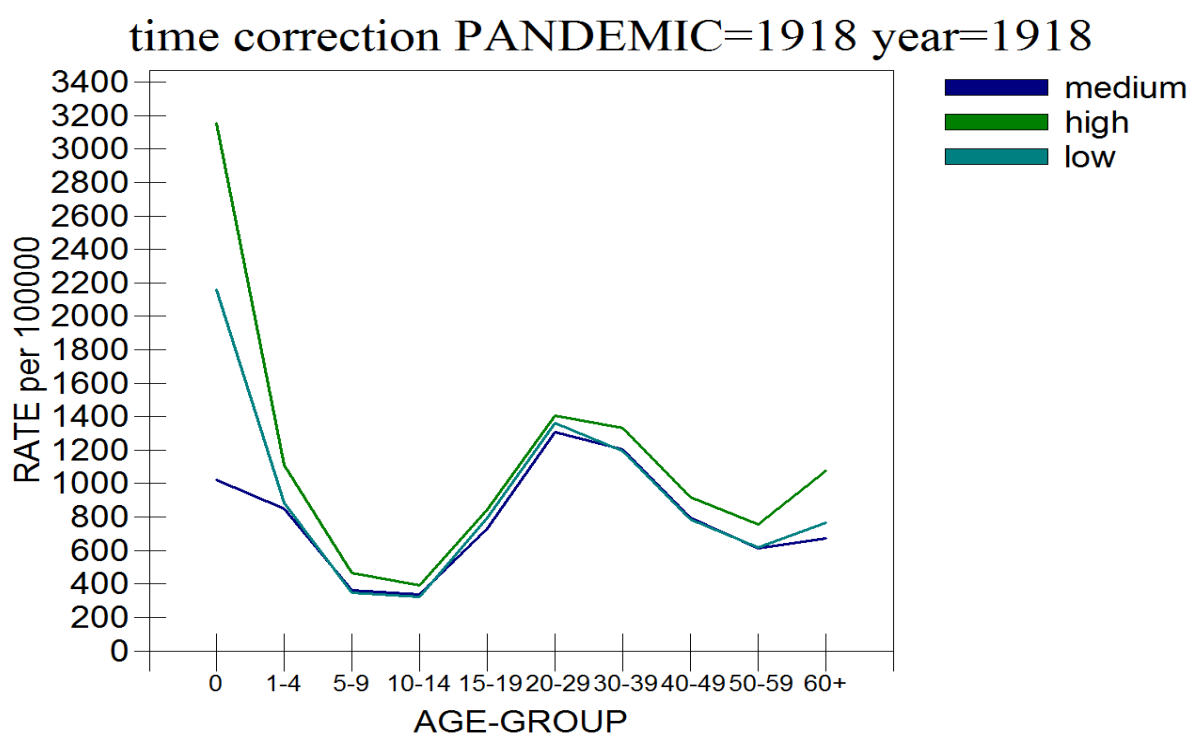
Web Figure 3A-3E .

Excess mortality rates per age group in 1918 result for models with less control variables and all two 1919 figures.

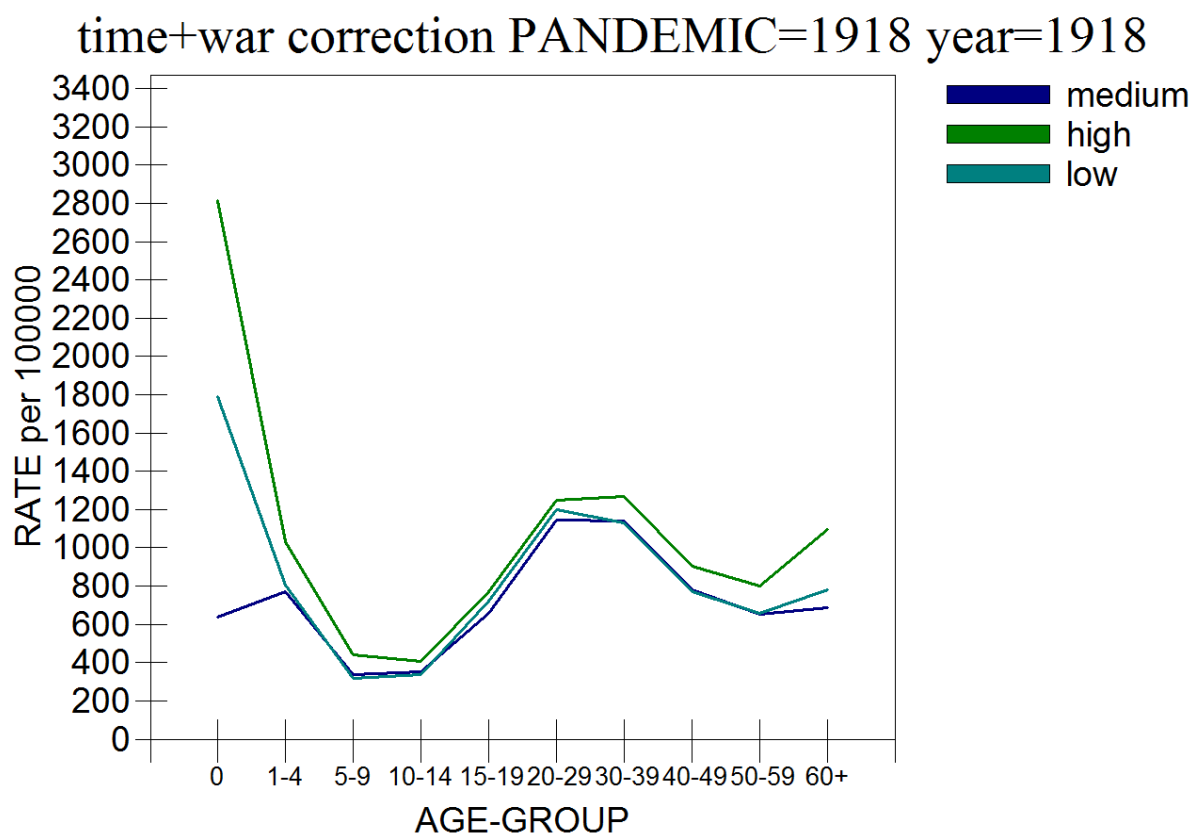
Web Figure 3A



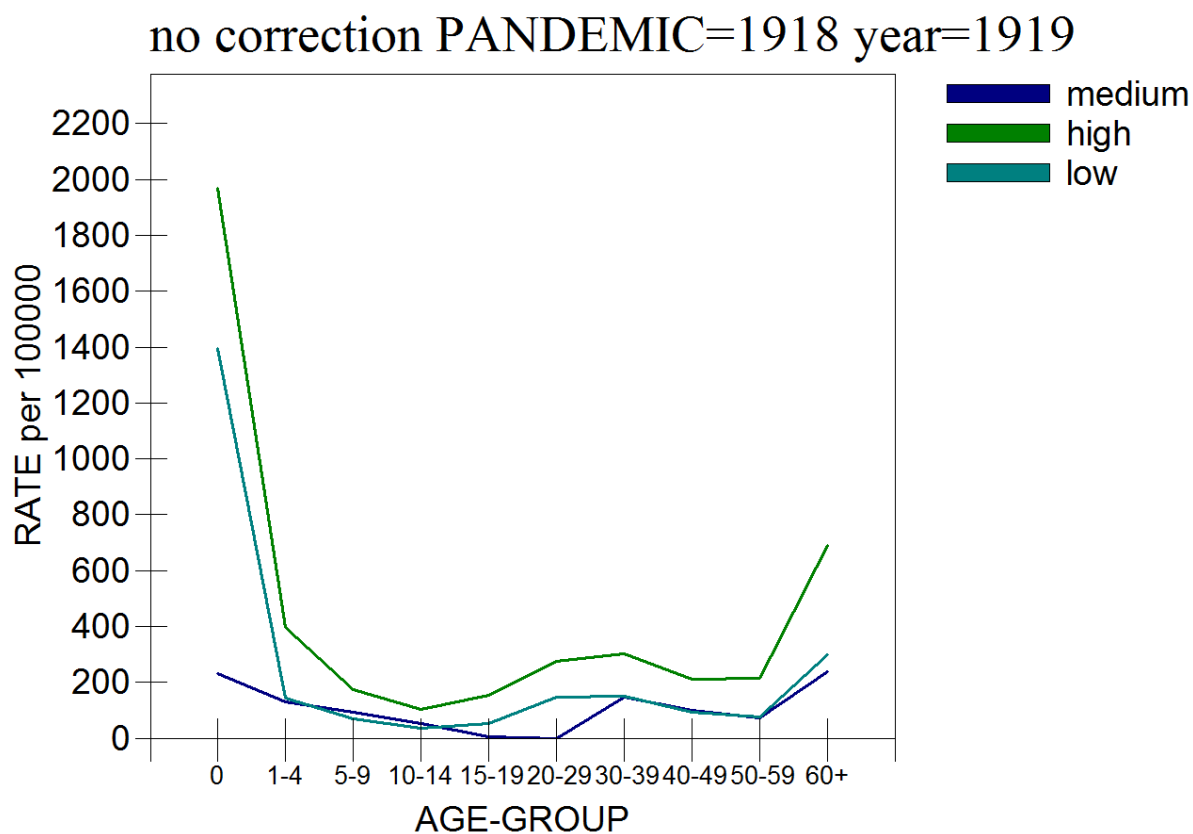
Web Figure 3B



Web Figure 3C

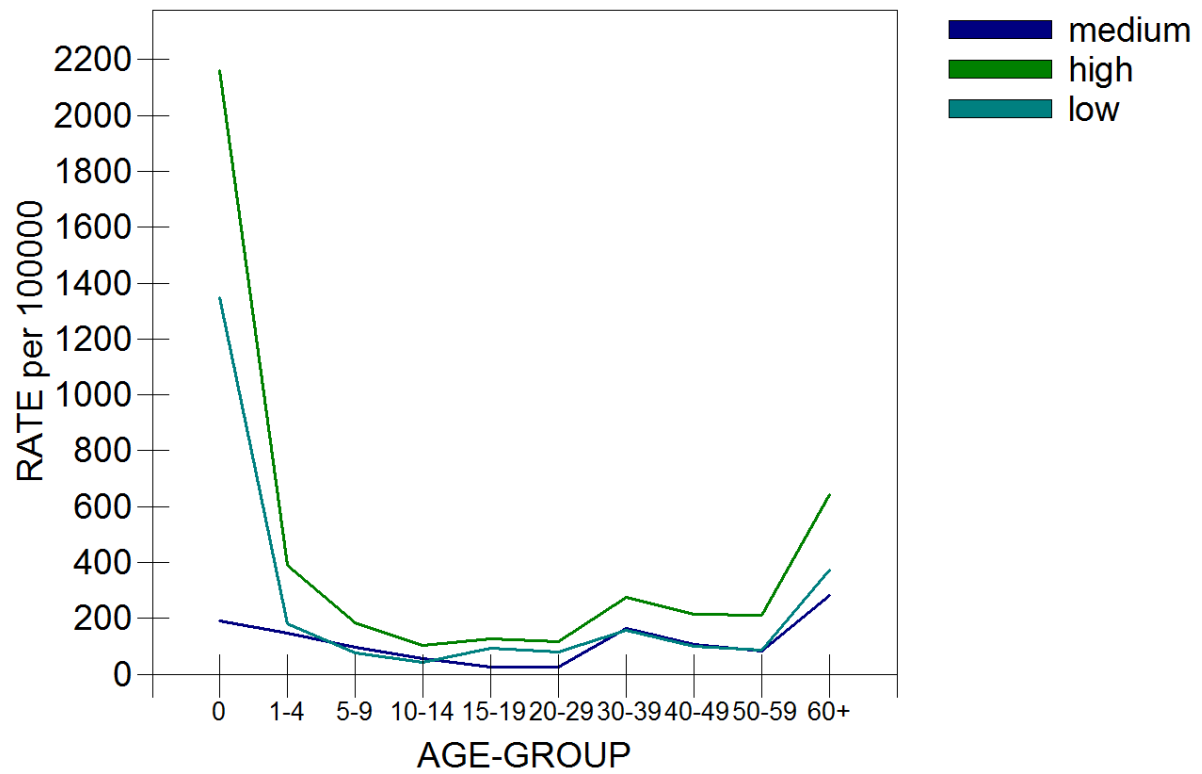


Web Figure 3D



Web Figure 3E

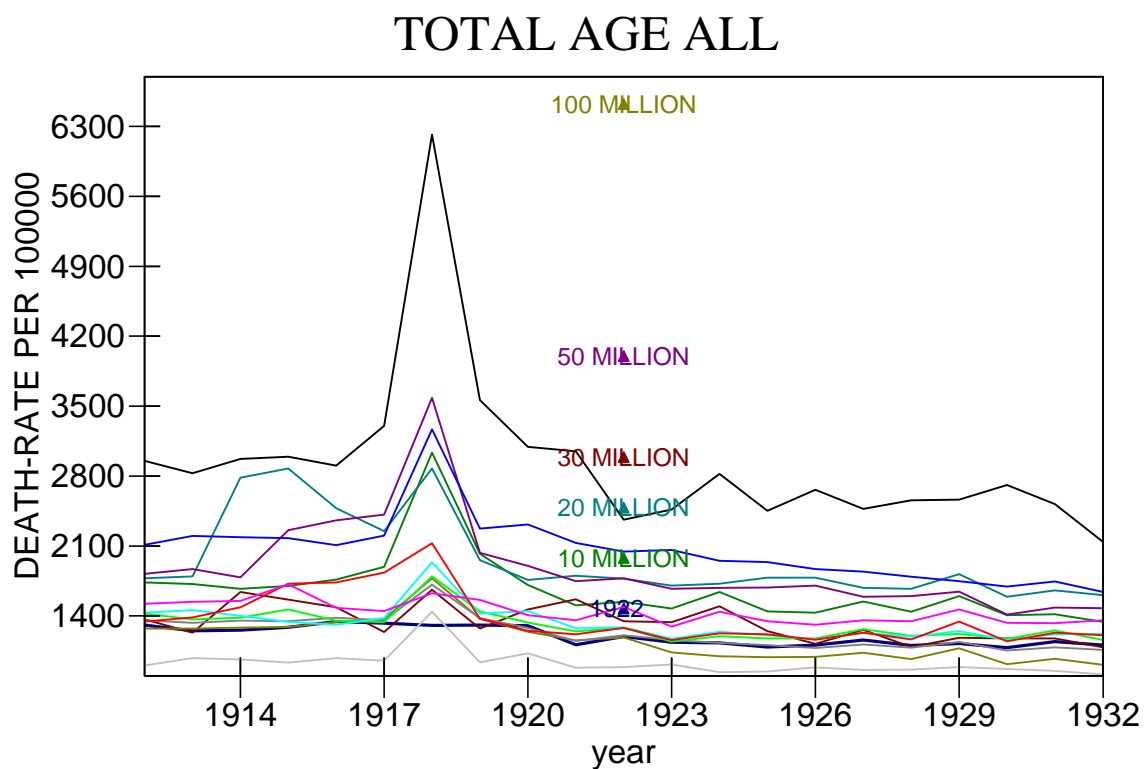
time correction PANDEMIC=1918 year=1919



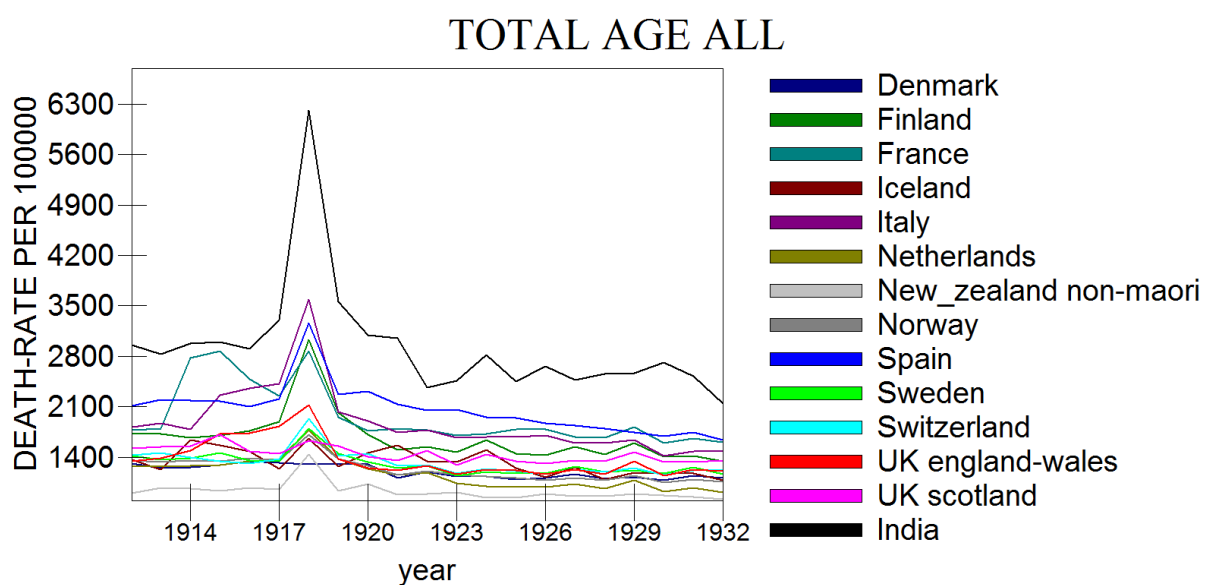
Web Figure 4A-4B.

graph showing the effect of different simulated excess death rates on the world death-rate.

Web Figure 4A



Web Figure 4B



Web Appendix 2.

Additional global burden estimates for the other pandemics.

We only present results per year based on the three scenario's. To choose between or combining scenario's is something that should be done for every pandemic separately. Which means study age specific results (see after these tables) for overestimation in the young and elderly (depends on the pandemic excess mortality theory for instance the age distribution for that pandemic), study sample data (see HMD data source), study per country if other reasons for excess mortality in the relevant years exist that should have been corrected for. So the results below are very premature results.

Also note the very strong effect of correcting for the non-stationarity in the time series in the Mexican pandemic 2009/2010 for the low and high scenario. The estimates in the tables below are based on the 10 age groups. But for the 2009 pandemic the results differ much from the literature (14). If 20 age group would be used results would be more in line with the literature (for 2009, low scenario and correcting for time-trend, 257222 deaths globally). So the choice of the age groups can be very important. Sometimes one could even consider to change the excess mortality for certain age groups to 0 if good theory expects results to be 0 in such an age group.

Smallpox pandemic years is based on the sample countries (mainly European), but in other parts of the world it maybe 1-2 years earlier or later (23). The purpose here is to put the 1918 pandemic into perspective, compare it with another infectious epidemic that causes a strong increase in mortality in 1-2 years in many countries (what would be the global burden if we can assume that the epidemic occurred globally).

Web Table 3.

table results based on model without correction for time trend.

NO CORRECTION		LOW		MEDIUM		HIGH	
PANDEMIC (NUMBER HMD COUNTRIES IN SAMPLE)	YEAR	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT
ASIAN (35)	1957	70.1	2.03M	29	840293	90.5	2.62M
	1958	13.2	387077	0	0	33.4	982659
HONGKONG (36)	1968	25	880890	6.6	231839	49.9	1.76M
	1969	39.6	1.42M	21.8	781780	64.7	2.32M
MEXICAN (40)	2009	35.5	2.42M	0.78	52977	53.1	3.63M
	2010	23.4	1.62M	0	0	41.6	2.85M
RUSSIAN (12)	1889	66.9	1.01M	0	0	107.9	1.63M
	1890	244.4	3.71M	84.3	1.28M	285.8	4.34M
SMALL-POX (10)	1871	317.1	4.26M	205.5	2.76M	568.6	7.64M
	1872	158.5	2.14M	98	1.33M	397.8	5.38M

Web Table 4.

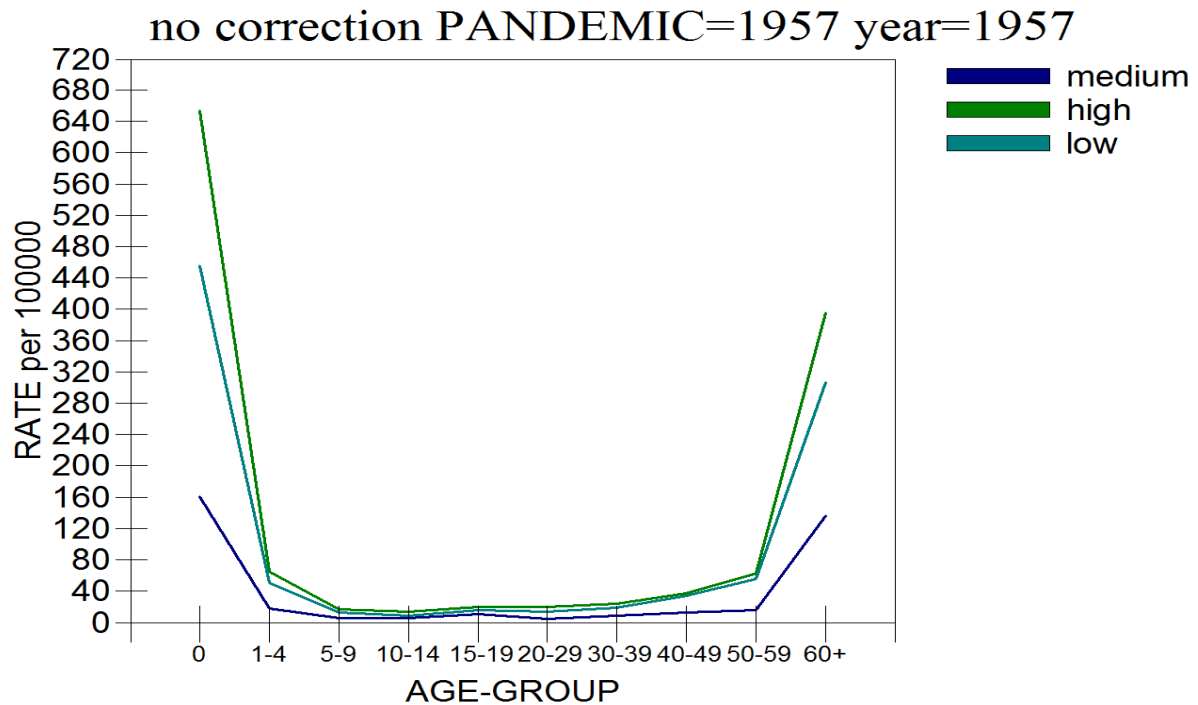
table results corrected for time trend.

TIME CORRECTED		LOW		MEDIUM		HIGH	
PANDEMIC (NUMBER HMD COUNTRIES IN SAMPLE)	YEAR	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT
ASIAN (35)	1957	51.9	1.51M	23.8	689907	70.1	2.06M
	1958	5.1	149859	0.04	1317	21.7	637232
HONGKONG (36)	1968	20.7	731004	7	247391	45.9	1.62M
	1969	35	1.26M	20.9	751697	60.5	2.17M
MEXICAN (40)	2009	0.8	55285	0.02	1057	11.9	811002
	2010	1.1	74259	0.3	1902	15.32	1.06M
RUSSIAN (12)	1889	41.3	622821	0	0	79.9	1.21M
	1890	203	3.08M	79.6	1.21M	252.4	3.84M
SMALL-POX (10)	1871	332.7	4.47M	187.2	2.52M	531.3	7.14M
	1872	204.6	2.77M	109.1	1.48M	387.7	5.24M

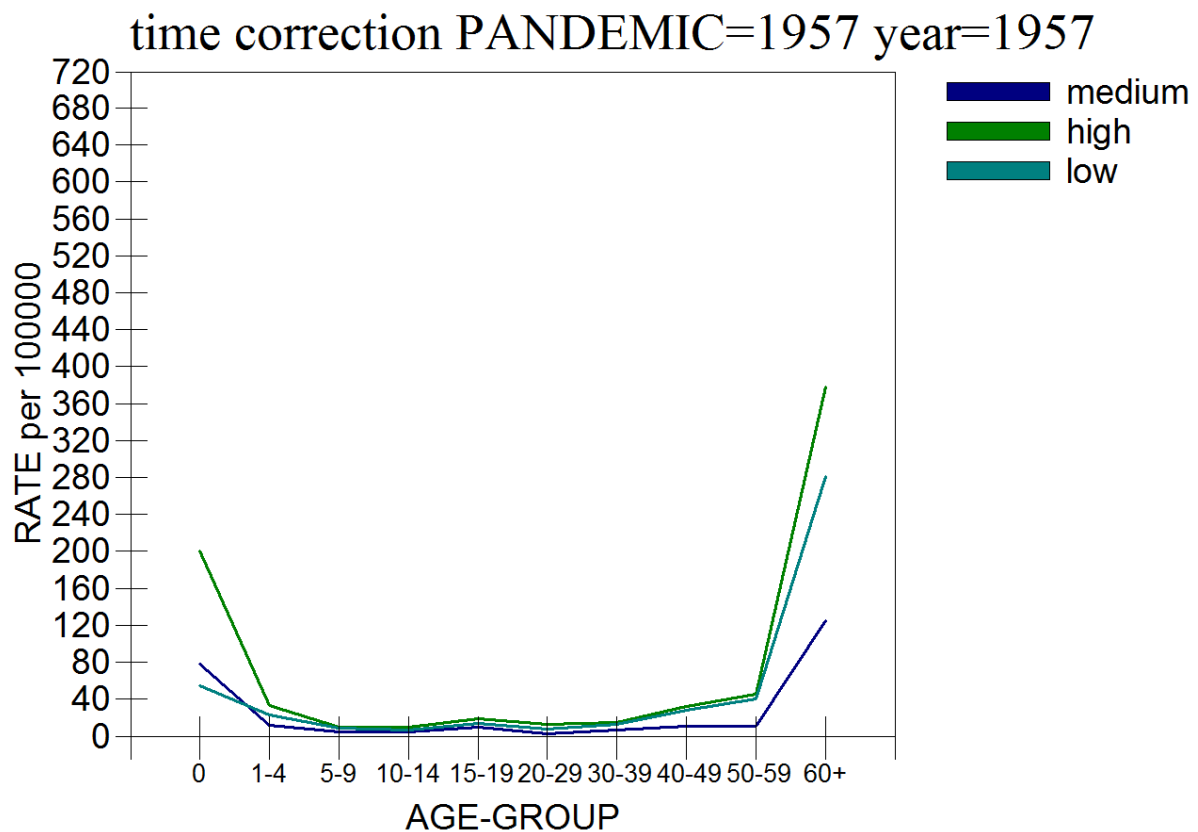
Web Figure 5A-5T.

Additional material for the other pandemics, excess mortality rates per age group.

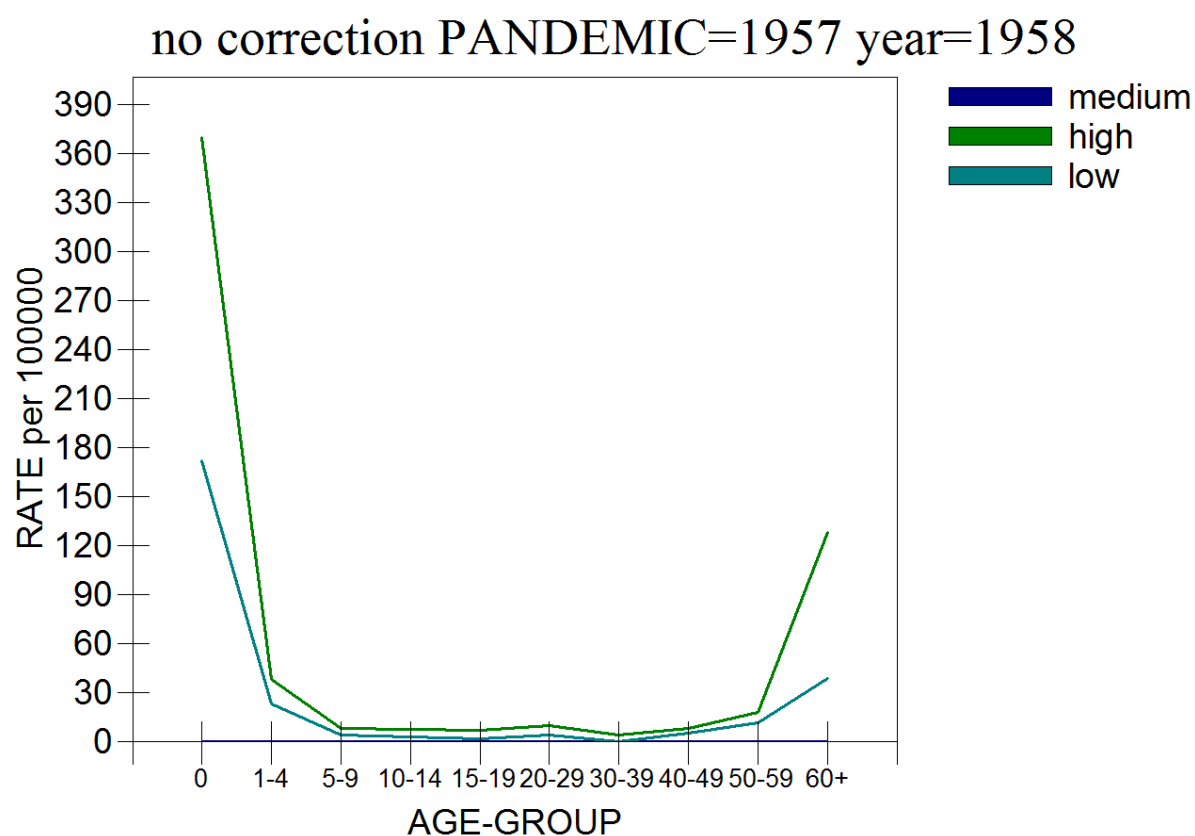
Web Figure 5A



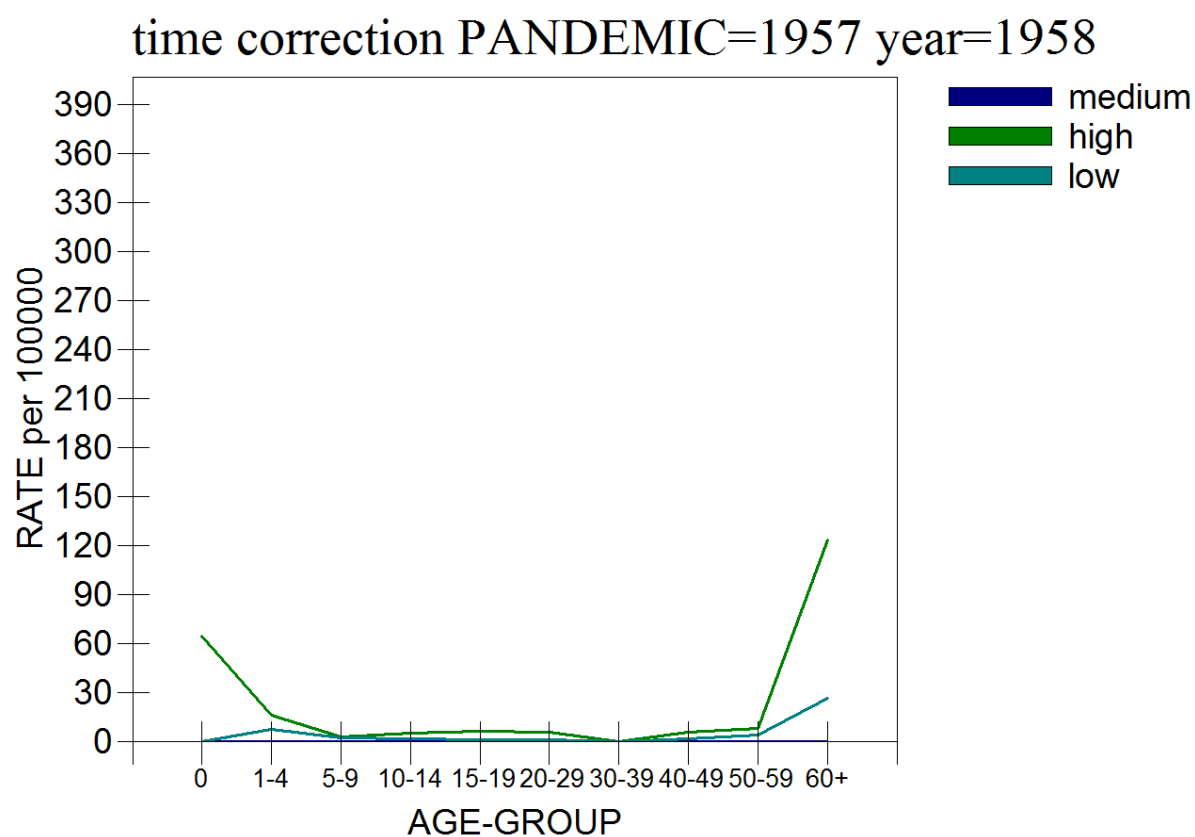
Web Figure 5B



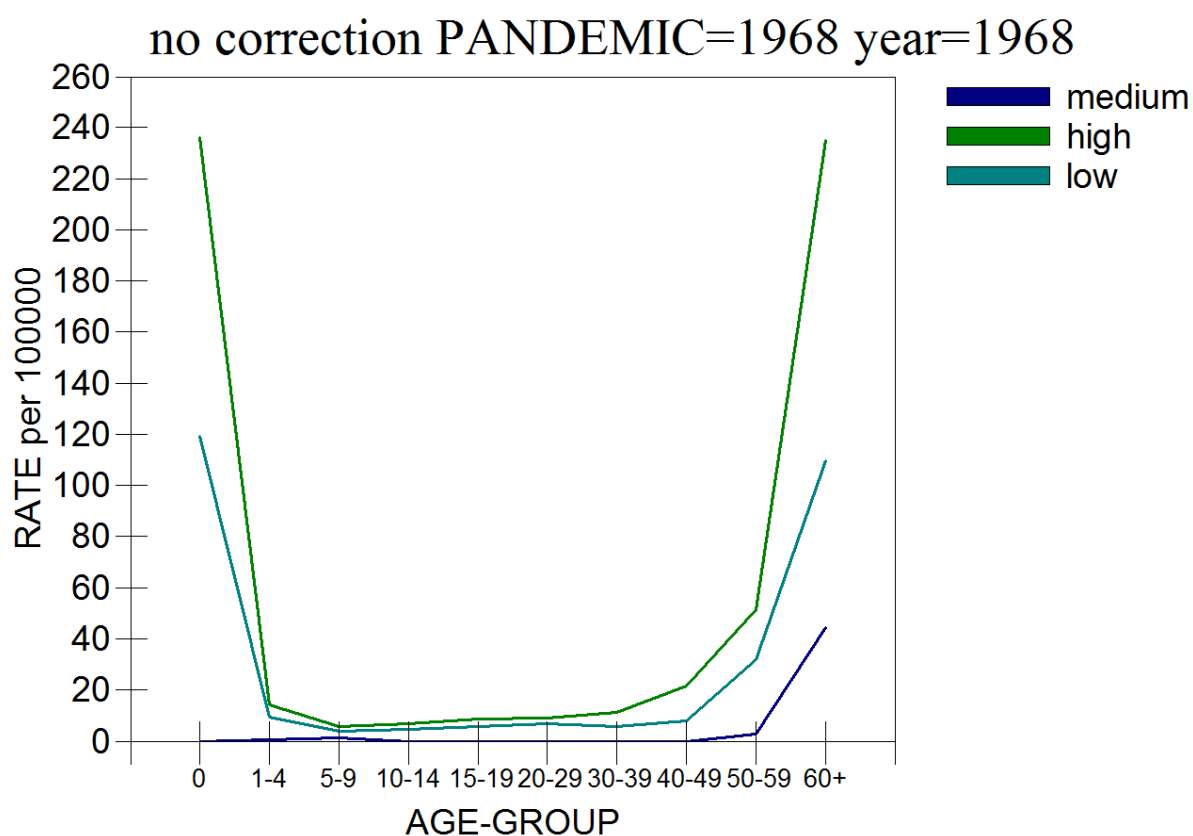
Web Figure 5C



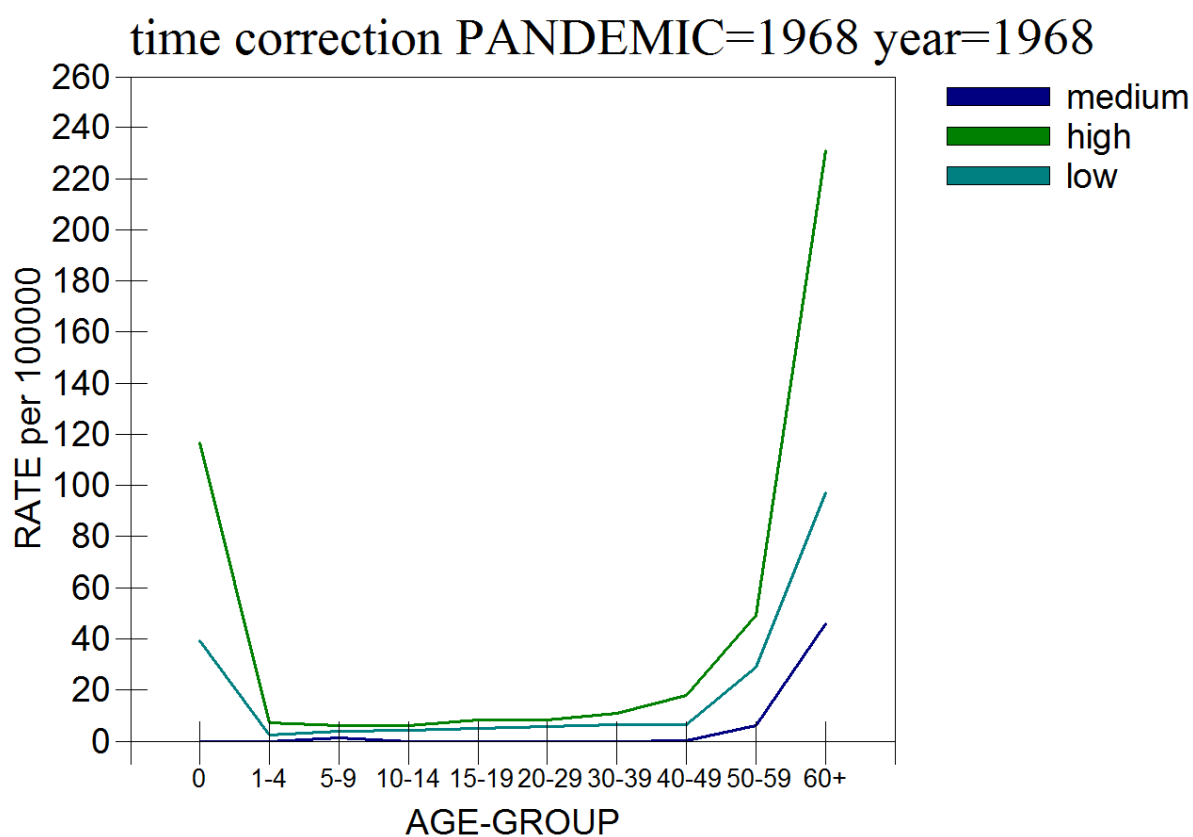
Web Figure 5D



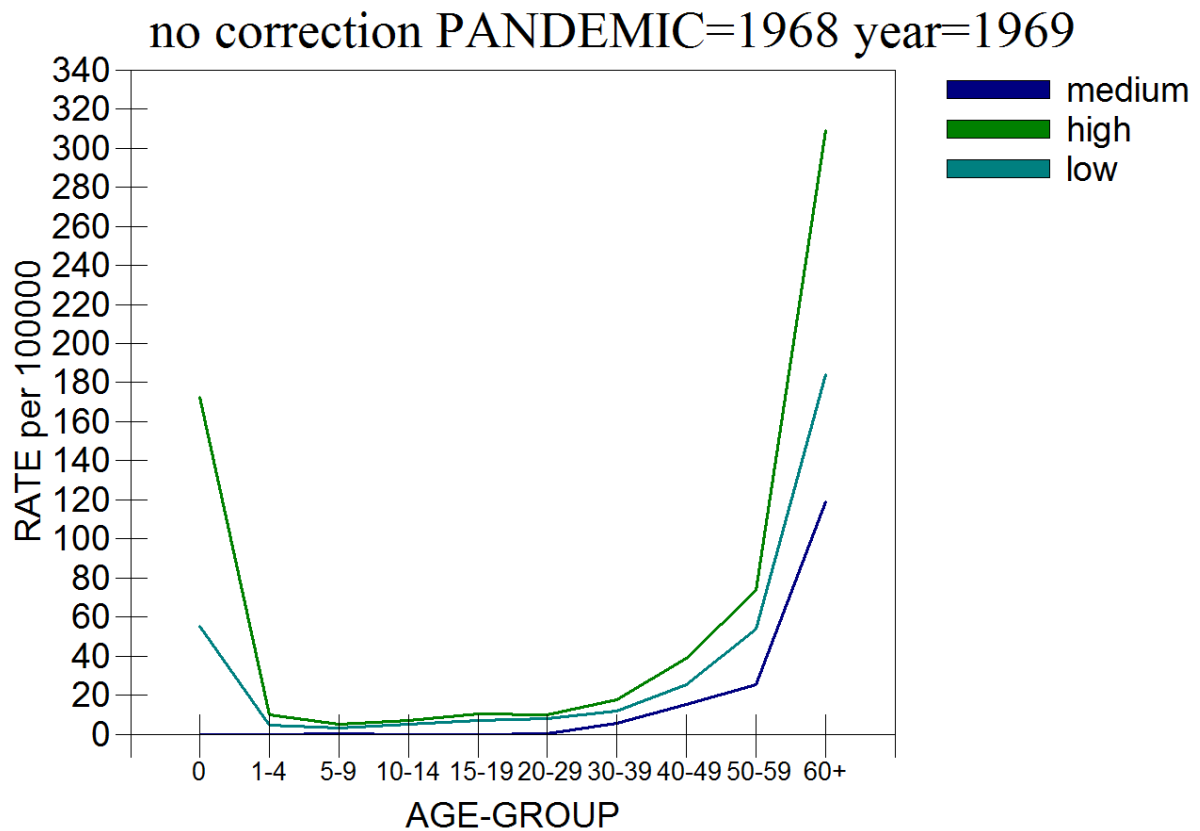
Web Figure 5E



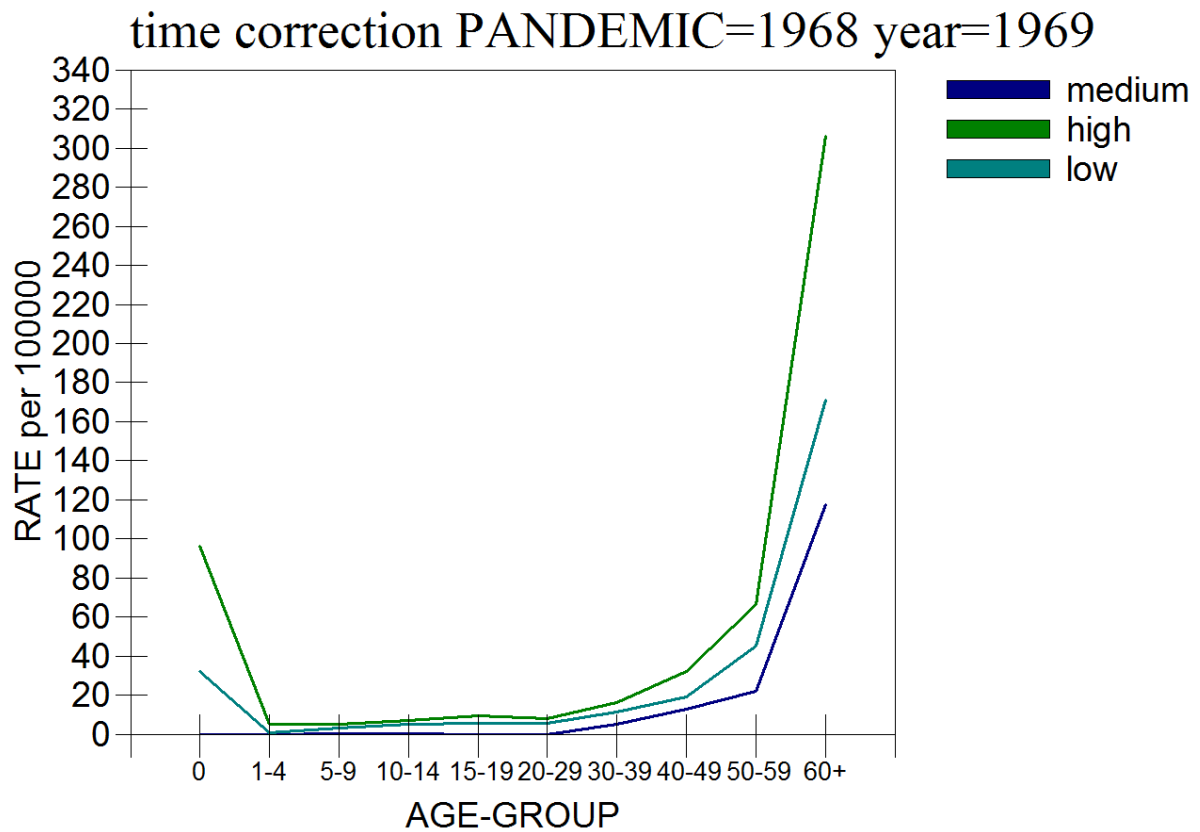
Web Figure 5F



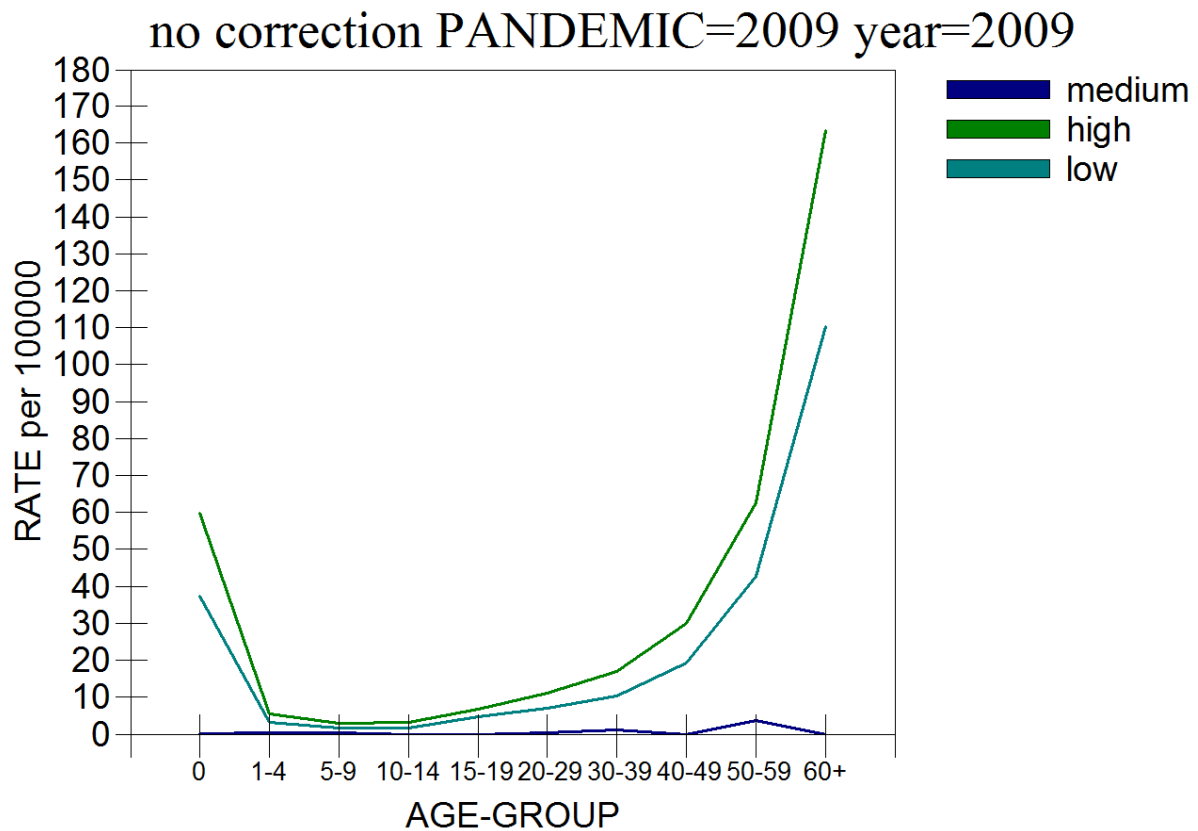
Web Figure 5G



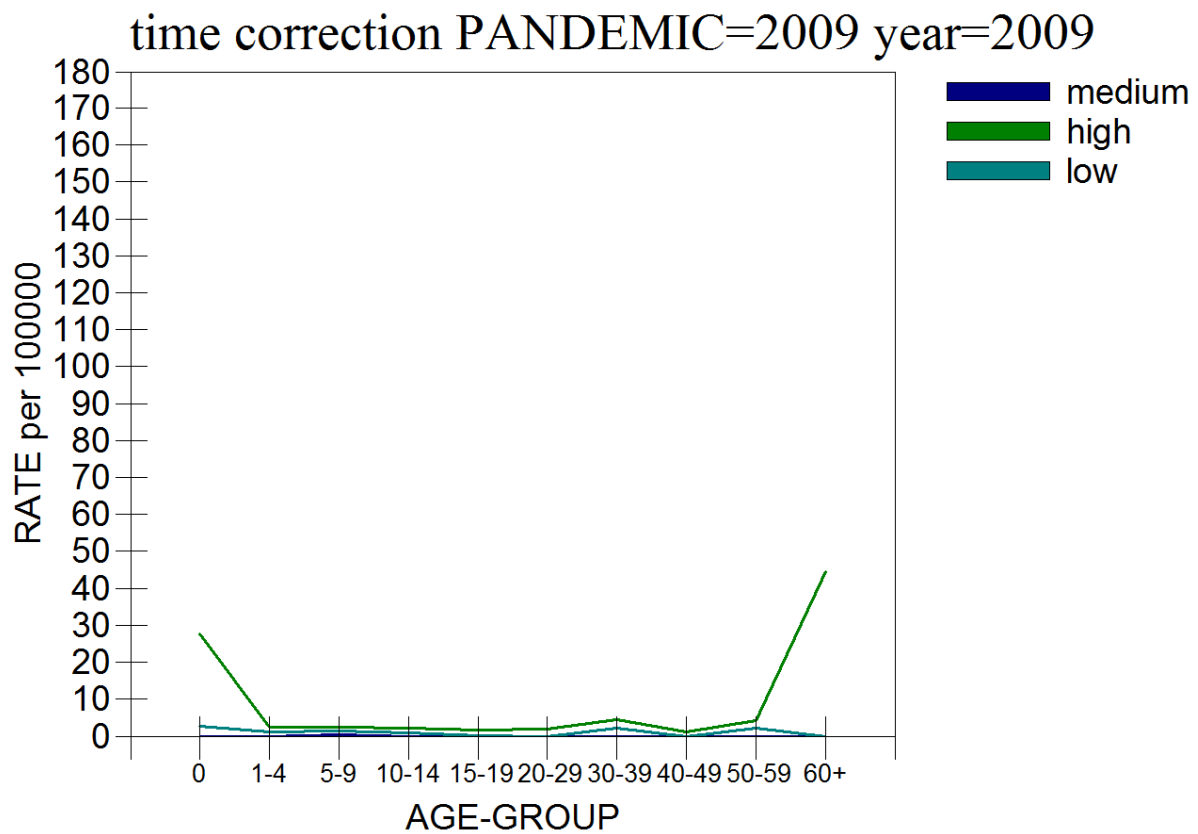
Web Figure 5H



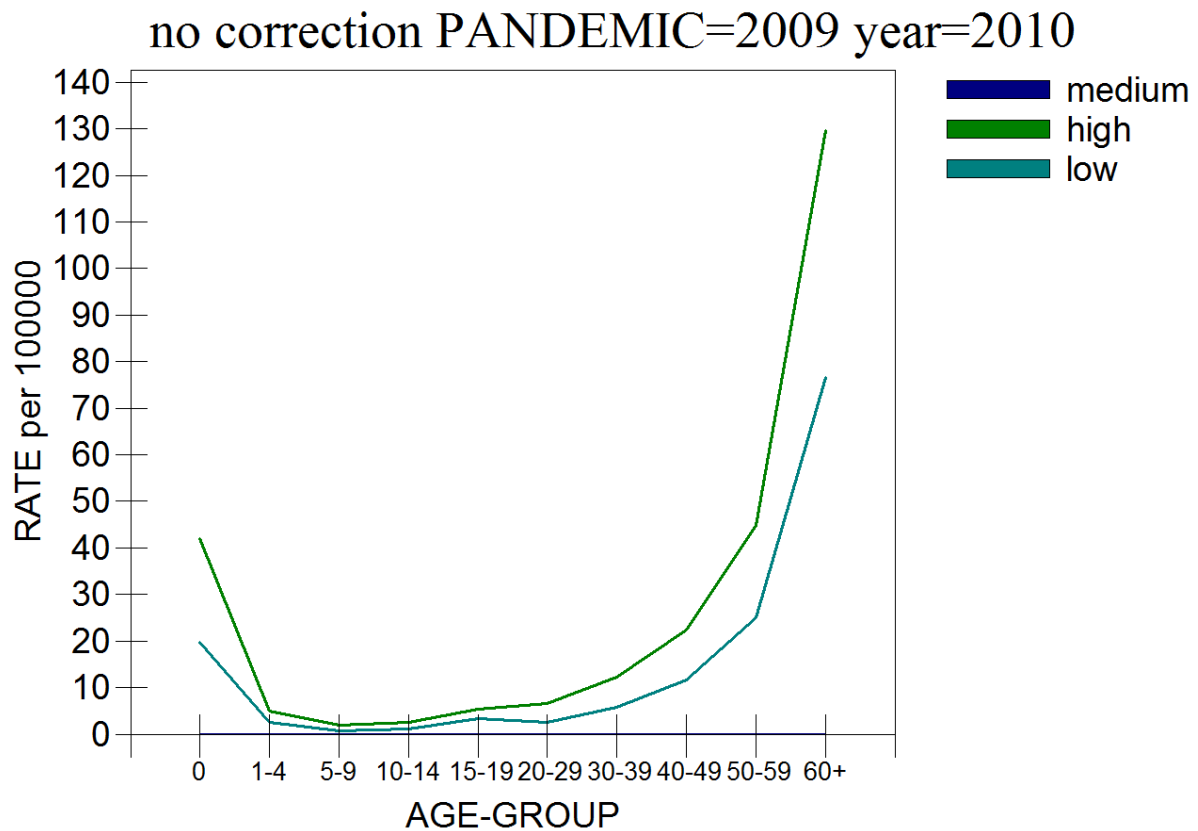
Web Figure 5I



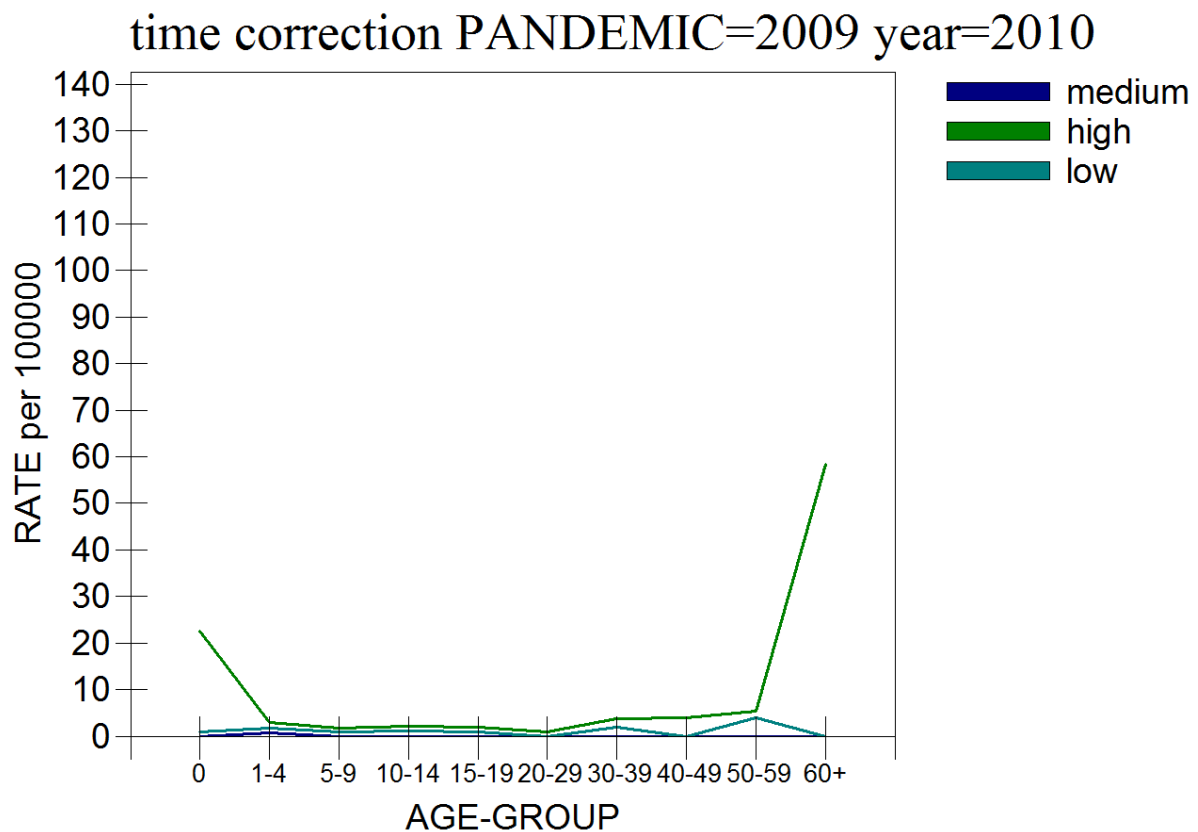
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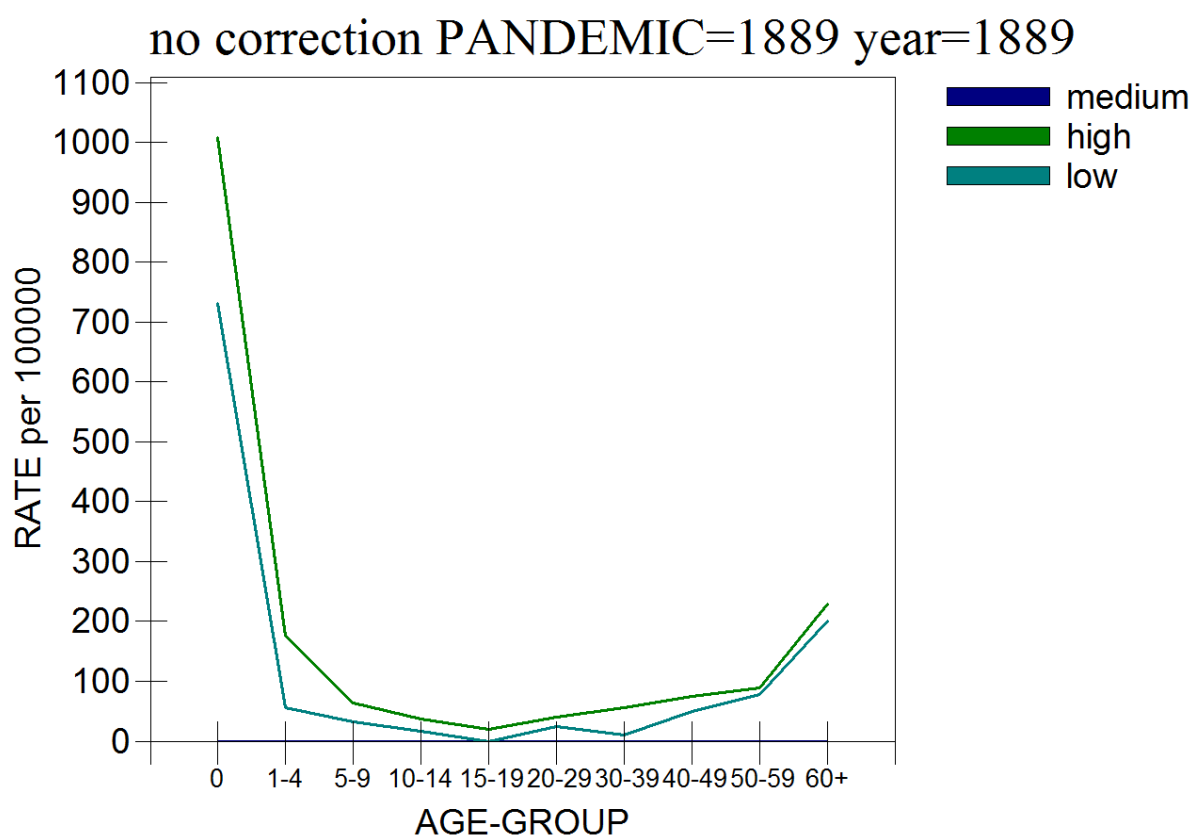
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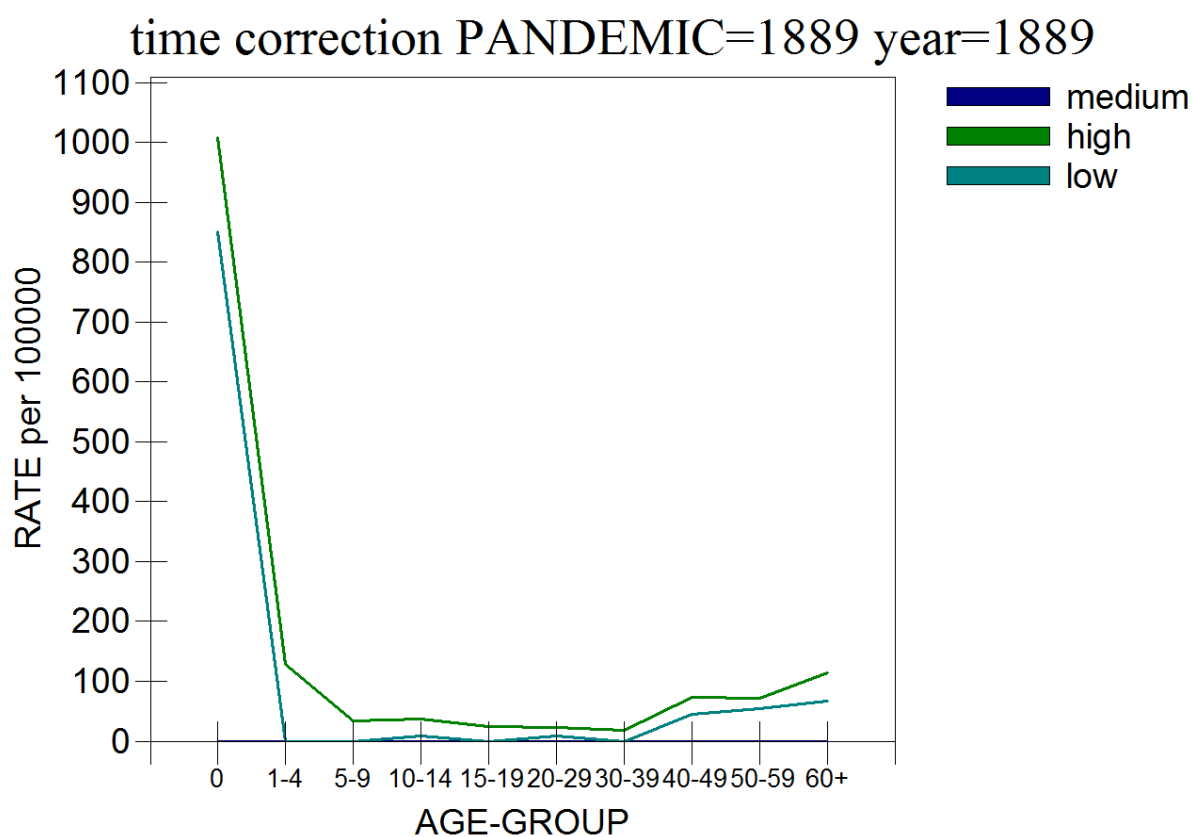
Web Figure 5L



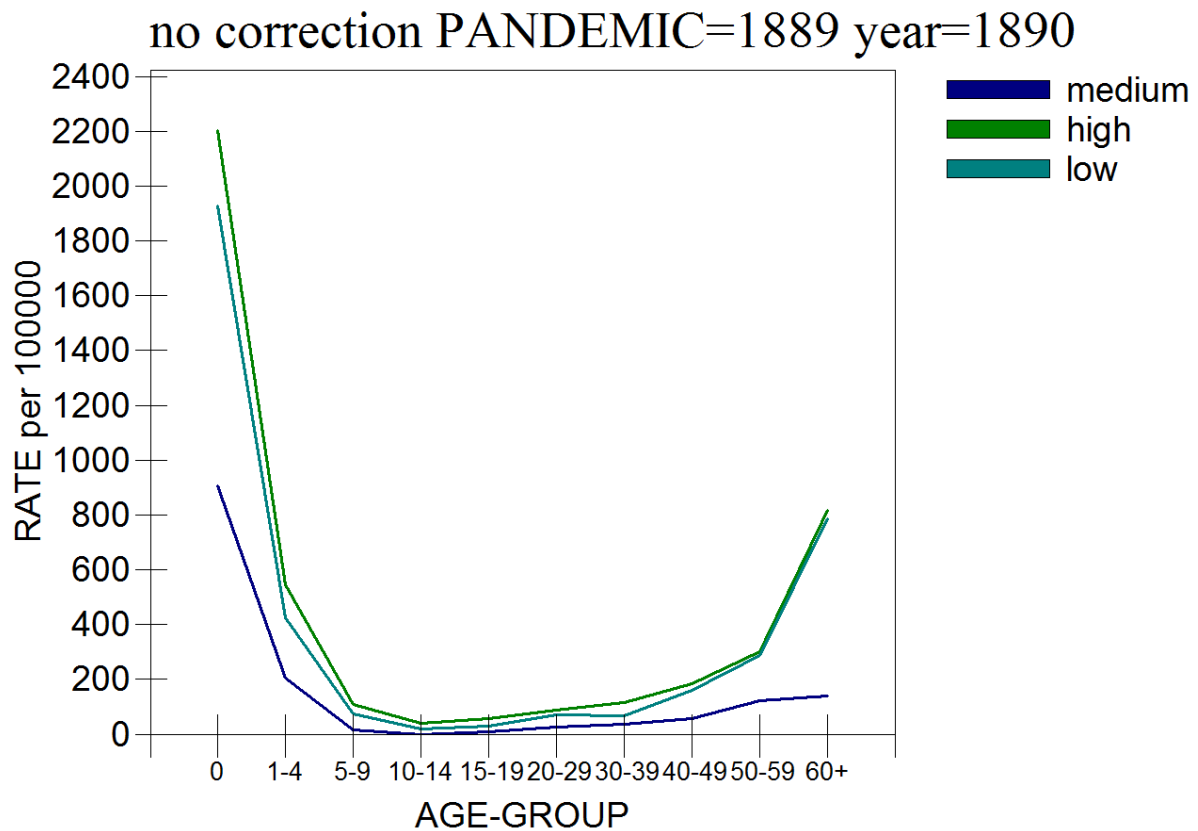
Web Figure 5M



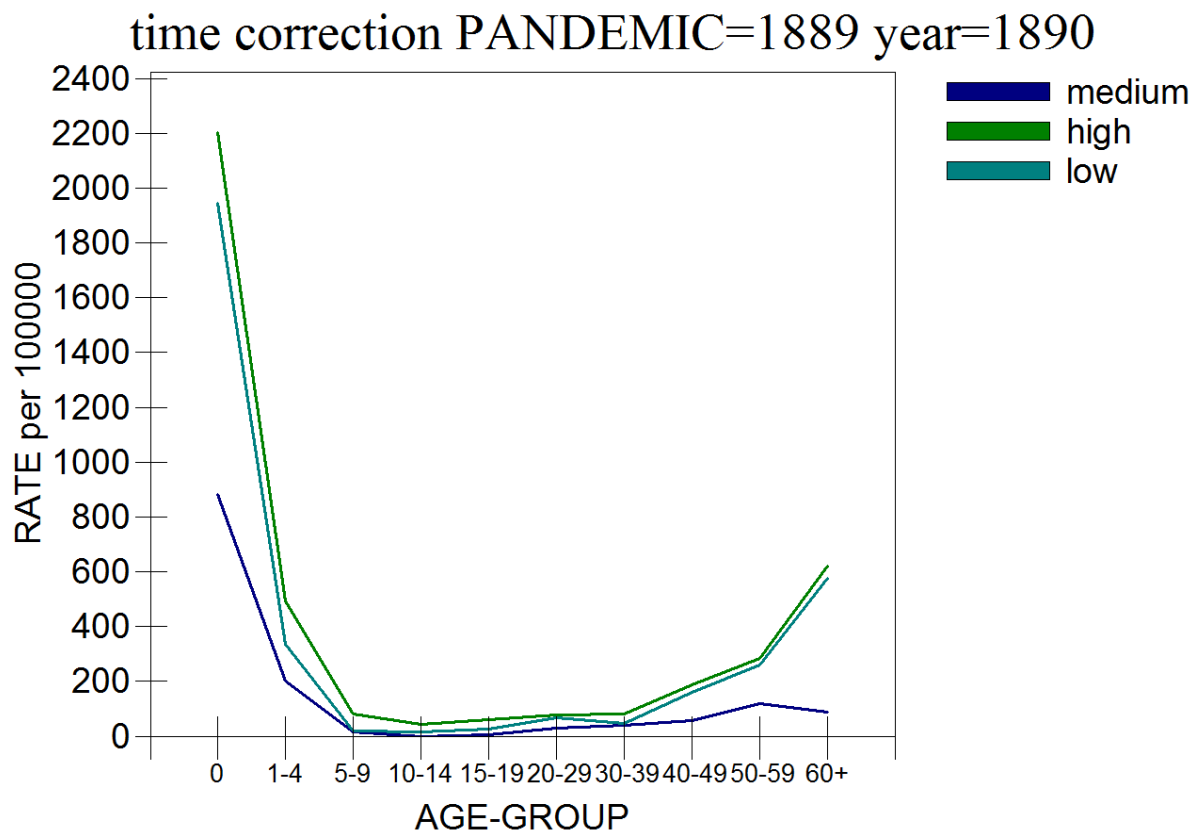
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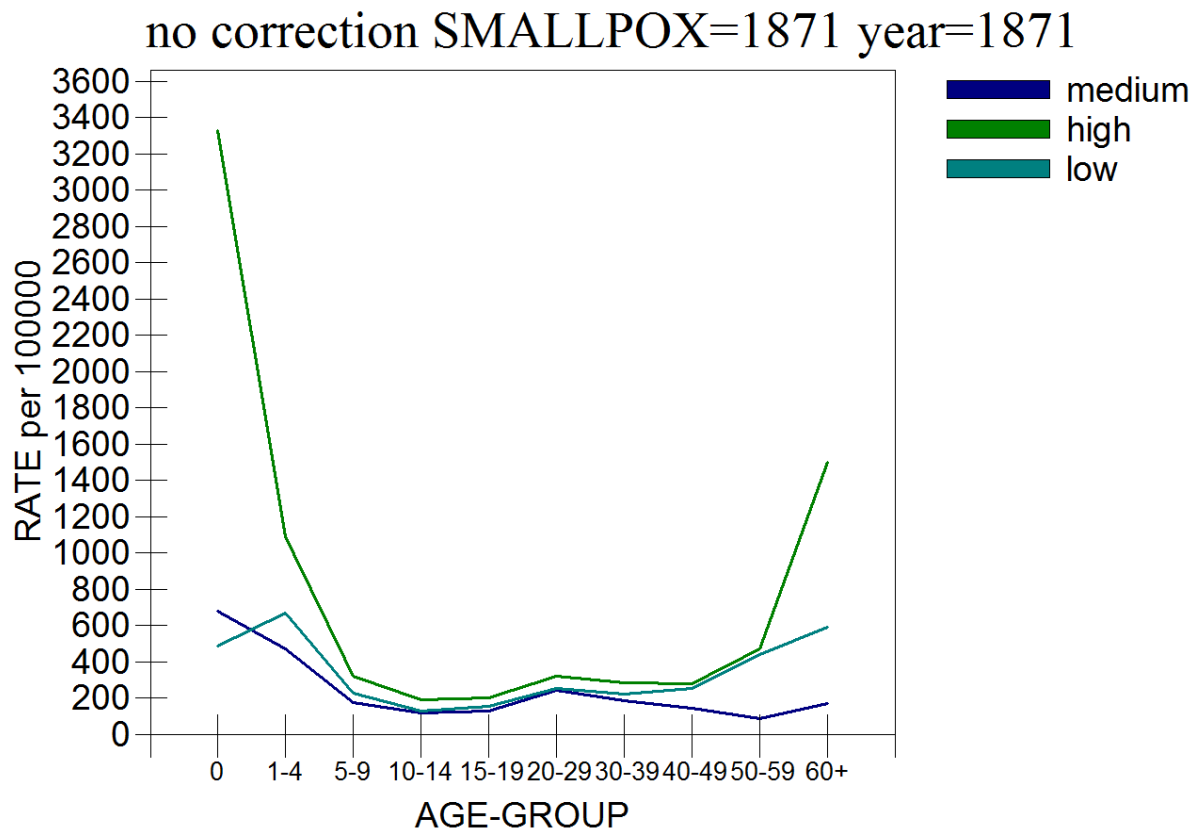
Web Figure 5O



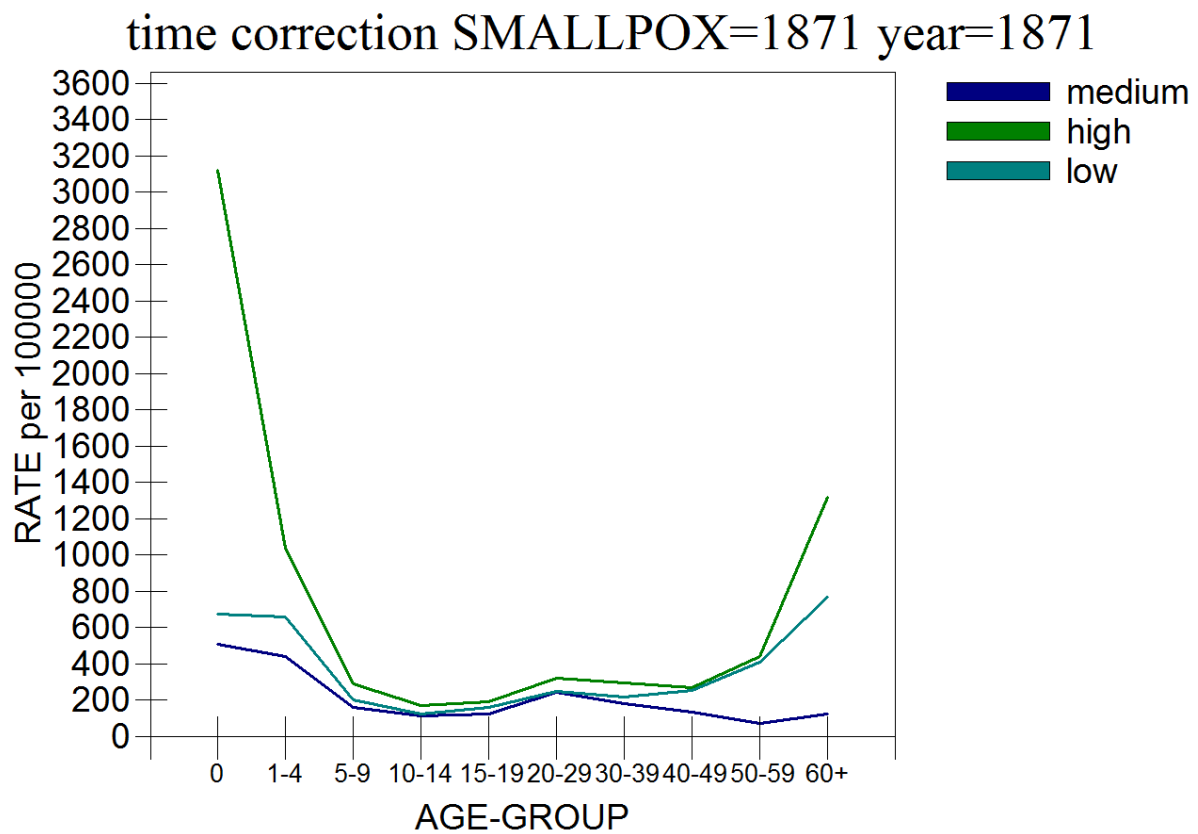
Web Figure 5P



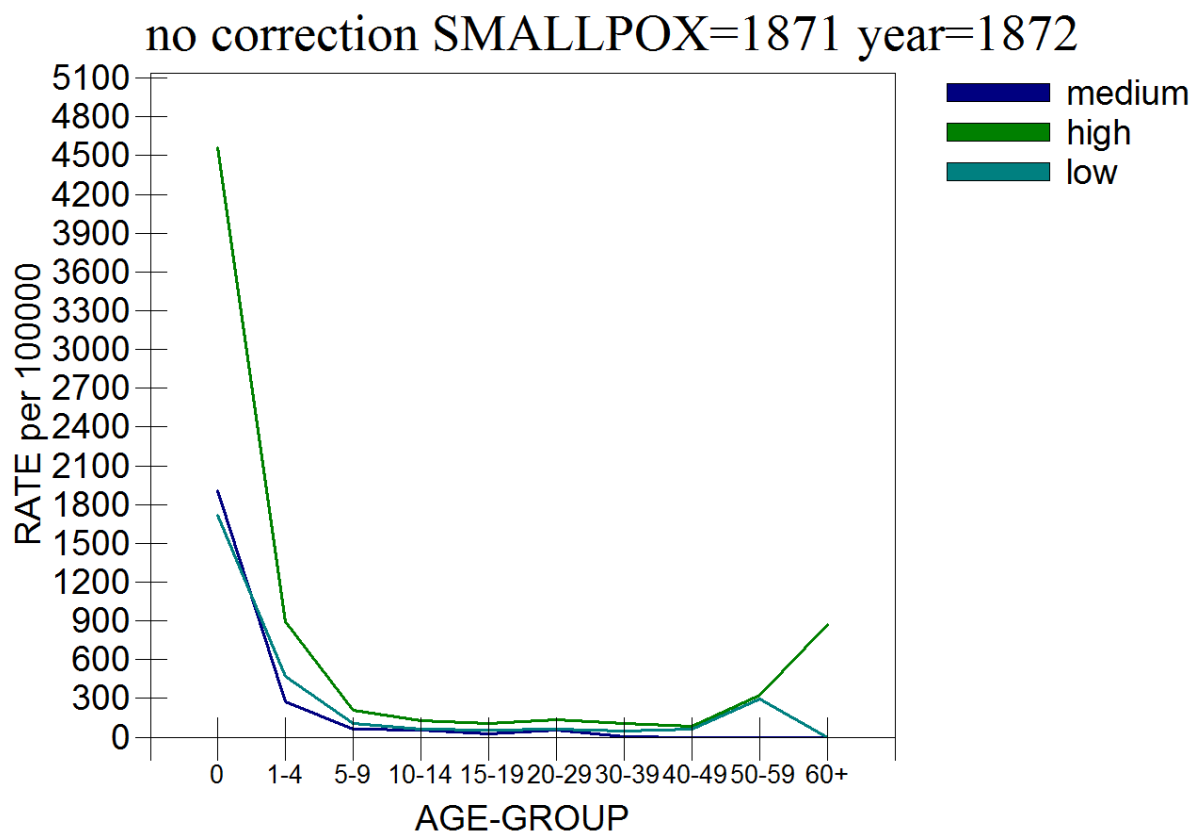
Web Figure 5Q



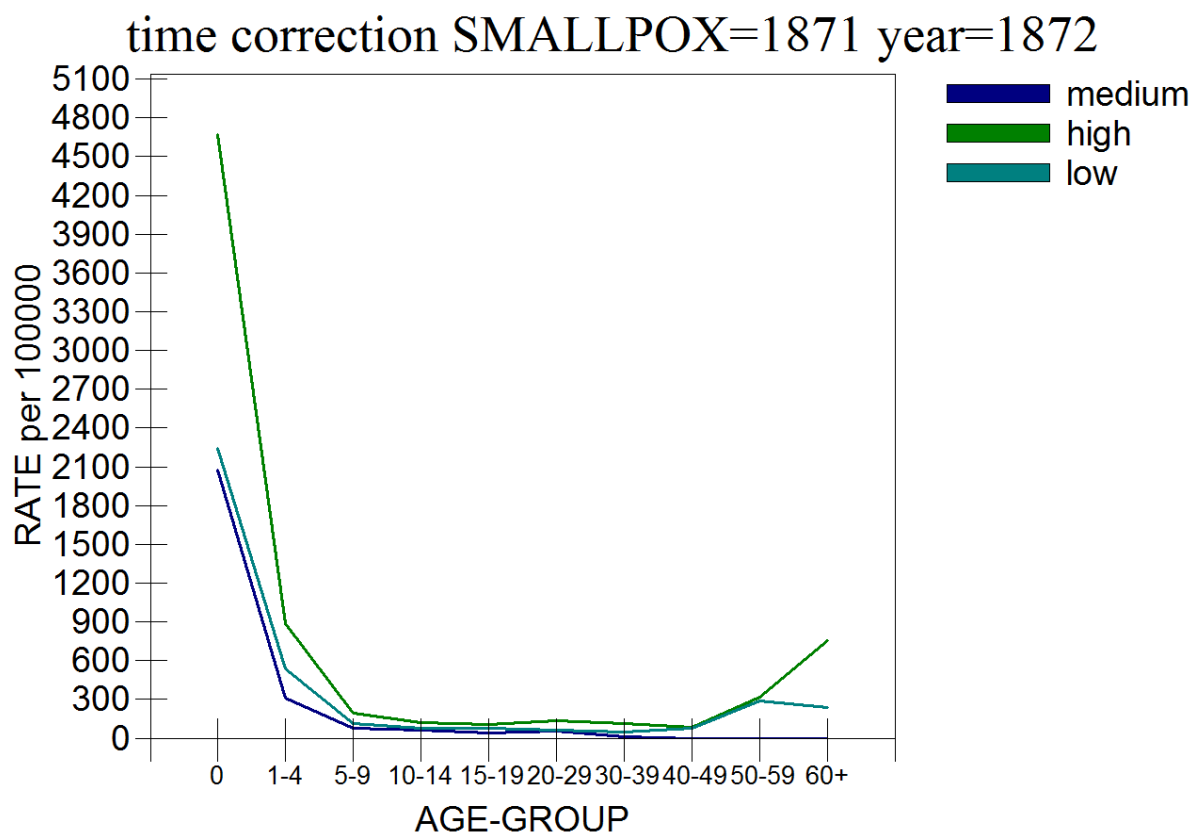
Web Figure 5R



Web Figure 5S

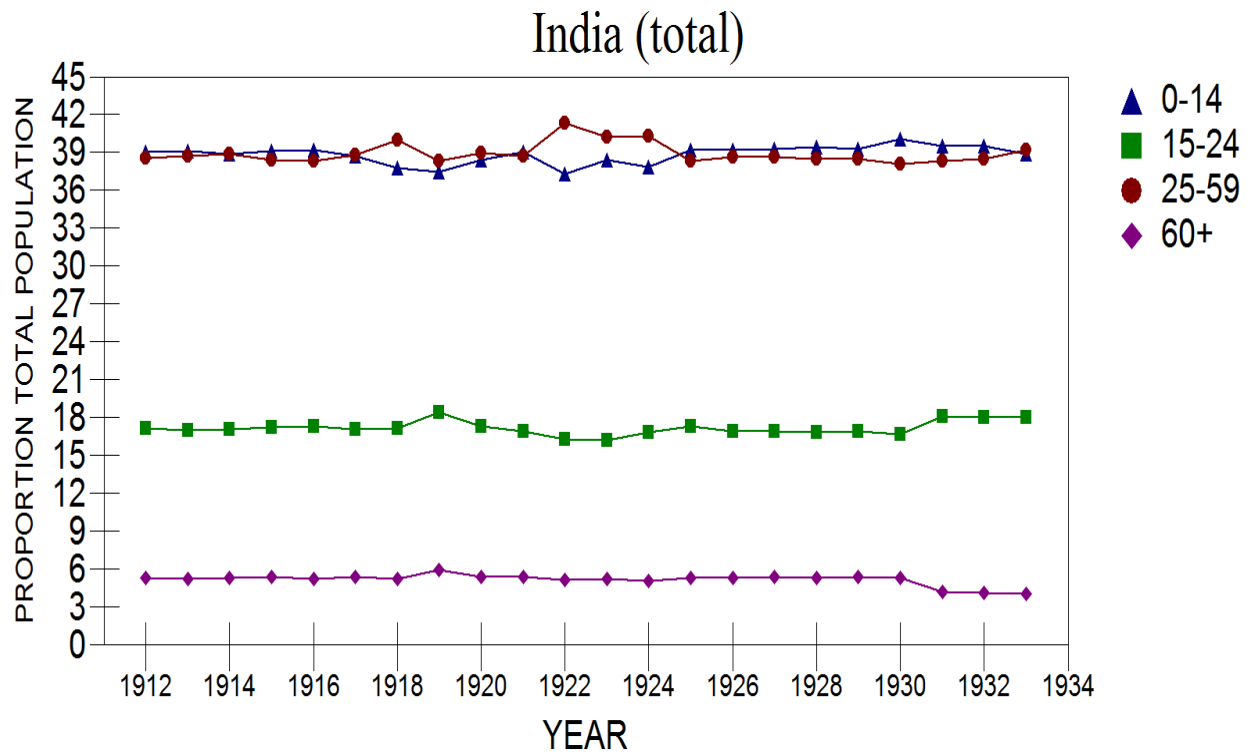


Web Figure 5T



Web Figure 6.

Relative contribution of four age groups in a series of years in India.



Web Table 5.

Individual country estimates for the three scenario's using the direct calculation method, country results are the pooled estimates from the 10 age categories. So these estimates are NOT corrected for time trend and war.

DIRECT CALCULATION		LOW		MEDIUM		HIGH	
COUNTRY	YEAR	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT	RATE PER 100000	DEATH COUNT
Denmark	1918	146.2	4,373	187.1	5,597	273.0	8,167
Denmark	1919	33.0	999	80.3	2,432	214.3	6,486
Finland	1918	1135.2	35,571	1,317.2	41,274	1,563.3	48,984
Finland	1919	165.1	5,141	318.0	9,903	561.6	17,489
France	1918	298.1	96,810	835.1	271,178	1,241.8	403,273
France	1919	2.2	723	17.0	5,508	294.4	95,538
Iceland	1918	251.3	230	315.3	288	500.5	457
Iceland	1919	0.0	0	0.0	0	94.9	87
Italy	1918	1055.0	387,165	1,560.8	572,752	1,968.6	722,428
Italy	1919	108.8	39,185	222.1	80,003	463.1	166,815
Netherlands	1918	411.1	27,207	501.2	33,173	635.3	42,043
Netherlands	1919	44.2	2,951	113.0	7,539	241.8	16,138
New_zealand non-maori	1918	430.6	4,883	498.2	5,650	568.2	6,444
New_zealand non-maori	1919	0.0	0	25.9	299	75.8	875
Norway	1918	349.0	8,956	417.8	10,719	570.4	14,634
Norway	1919	38.9	1,007	93.7	2,427	235.6	6,100
Spain	1918	877.4	186,888	1,058.8	225,517	1,240.6	264,251
Spain	1919	39.6	8,404	125.6	26,689	260.4	55,319
Sweden	1918	440.0	25,531	497.3	28,856	582.6	33,800
Sweden	1919	74.7	4,346	133.8	7,779	227.6	13,236
Switzerland	1918	487.9	18,924	591.7	22,948	701.0	27,189
Switzerland	1919	5.7	220	71.7	2,772	179.8	6,947
UK england-wales	1918	309.9	116,073	651.7	244,069	998.2	373,858
UK england-wales	1919	3.4	1,254	47.3	17,582	237.6	88,382
UK scotland	1918	184.5	8,879	246.8	11,878	343.1	16,514
UK scotland	1919	50.0	2,411	165.5	7,977	274.5	13,233
India	1918	2926.9	7,105,507	3,140.4	7,623,998	3,399.3	8,252,450
India	1919	370.3	907,583	548.9	1,345,227	806.8	1,977,222